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ECBC-TR-407

LOW-LEVEL CYCLOSARIN (GF) VAPOR EXPOSURE IN RATS: EFFECT OF EXPOSURE CONCENTRATION AND DURATION ON PUPIL SIZE

Christopher E. Whalley
Bernard J. Benton
James H. Manthei
Ruth A. Way
Edward M. Jakubowski, Jr.
David C. Burnett
Bernardita I. Gaviola
Ronald B. Crosier
Douglas R. Sommerville
William T. Muse
Jeffry S. Forster
Robert J. Mioduszewski
Sandra A. Thomson

RESEARCH AND TECHNOLOGY DIRECTORATE

Jacqueline A. Scotto
Dennis B. Miller
Charles L. Crouse
Kathy L. Matson
Jennifer L. Edwards

GEO-CENTERS

GEO-CENTERS, INC.
Abingdon, MD 21009

September 2004

ABERDEEN PROVING GROUND, MD 21010-5424

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REPORT DOCUMENTATION PAGE

Form Approved
OMB No. 0704-0188

1. REPORT DATE (DD-MM-YYYY)	2. REPORT TYPE	3. DATES COVERED (From - To)
XX-09-2004	Final	Feb 2002 - Oct 2002

4. TITLE AND SUBTITLE
Low-Level Cyclosarin (GF) Vapor Exposure in Rats: Effect of Exposure Concentration and Duration on Pupil Size

5a. CONTRACT NUMBER

5b. GRANT NUMBER

5c. PROGRAM ELEMENT NUMBER

6. AUTHOR(S)
Whalley, Christopher E.; Benton, Bernard J.; Manthei, James H.; Way, Ruth A.; Jakubowski, Edward M.; Burnett, David C.; Gaviola, Bernardita, I.; Crosier, Ronald B.; Sommerville, Douglas R.; Muse, William T.; Forster, Jeffry S.; Mioduszewski, Robert J.; Thomson, Sandra A. (ECBC); Scotto, Jacqueline A.; Miller, Dennis B.; Crouse, Charles L.; Matson, Kathy L.; and Edwards, Jennifer L. (GEO-CENTERS, INC.)

5d. PROJECT NUMBER
206023

5e. TASK NUMBER

5f. WORK UNIT NUMBER

7. PERFORMING ORGANIZATION NAME(S) AND ADDRESS(ES) AND ADDRESS(ES)
DIR, ECBC, ATTN: AMSRD-ECB-RT-TT, APG, MD 21010-5424
GEO-CENTERS, Incorporated, Abingdon, MD 21009

8. PERFORMING ORGANIZATION REPORT NUMBER
ECBC-TR-407

9. SPONSORING / MONITORING AGENCY NAME(S) AND ADDRESS(ES)
Defense Threat Reduction Agency, 8725 John J. Kingman Road, MS 6201, Fort Belvoir, VA 22060-6201

10. SPONSOR/MONITOR'S ACRONYM(S)

11. SPONSOR/MONITOR'S REPORT NUMBER(S)

12. DISTRIBUTION / AVAILABILITY STATEMENT
Approved for public release; distribution is unlimited.

13. SUPPLEMENTARY NOTES

14. ABSTRACT

Probability of cyclosarin (GF) miosis (defined as post-exposure pupil diameter 50% or less of pre-exposure pupil diameter) was estimated in rats exposed to combinations of exposure concentration and duration. Groups of male and female rats were exposed to GF vapor for a single duration (10, 60, or 240 min) in a whole-body dynamic chamber. Pupil diameter was measured by infrared camera technique. For six combinations of gender and exposure duration, effective concentration for miosis in 50% of exposed population and common probit slope were determined. Contrary to Haber's rule, ECt50 values increased with exposure duration. Female rats were more sensitive to GF vapor toxicity than male rats. Miosis was the only clinical sign noted following GF vapor exposure. Mydriasis was not observed in the present study. Depression of blood esterase (acetylcholinesterase, butyrylcholinesterase, and carboxylesterase) activites due to low level range of GF vapor concentrations was also investigated. Cyclosarin was regenerated from blood samples of vapor-exposed rats by addition of fluoride ion at pH 4, and the samples were analyzed by GC-FPD and GC-MS. Levels of regenerated GF in red blood cell fraction of samples were 5 to 40 times lower than in plasma. All controls were negative for regenerated GF.

15. SUBJECT TERMS

Duration	Eye	Low level	Rats	Ct
Concentration	Miosis	Inhalation	Cyclosarin	GF

16. SECURITY CLASSIFICATION OF:			17. LIMITATION OF ABSTRACT	18. NUMBER OF PAGES	19a. NAME OF RESPONSIBLE PERSON
a. REPORT	b. ABSTRACT	c. THIS PAGE			Sandra J. Johnson
U	U	U	UL	68	19b. TELEPHONE NUMBER (include area code) (410) 436-2914

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PREFACE

The work described in this report was authorized under Project No. 206023, Low Level Toxicology. The work was started in February 2002 and completed in October 2002. The experimental data are contained in laboratory notebook 02-0010. Raw data and the final report from this study are stored in the Toxicology Archives (Building E-3150), online in Restech 'Filesvr' (G:\LLT\GF rat raw data Whalley protocol), and/or in the Technical Library (Building E-3330) Aberdeen Proving Ground, MD.

In conducting this study, investigators adhered to the "Guide for the Care and Use of Laboratory Animals," National Research Council, National Academy Press, 1996, as promulgated by the Committee on Revision of the Guide for Laboratory Animal Facilities and Care of the Institute of Laboratory Animal Resources, Commission of Life Sciences, National Research Council, Washington, DC. These investigations were also performed in accordance with the requirements of AR 70-18, "Laboratory Animals, Procurement, Transportation, Use, Care, and Public Affairs," and the U.S. Army Edgewood Chemical Biological Center (ECBC) Institutional Animal Care and Use Committee (IACUC), which oversees the use of laboratory animals. This project's assigned IACUC Protocol No. 02-338, was approved on 30 January 2002.

Studies were conducted under, and in compliance with, current GLP standards and they were reviewed periodically by the QA Coordinator or his designee.

The performance of this study was consistent with the objectives and standards in "Good Laboratory Practices for Non-clinical Laboratory Studies" (21 CFR 58, Food and Drug Administration, U.S. Department of Health and Human Services, April 1988).

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Acknowledgments

The authors thank Dr. Julie Watson (GEO-CENTERS, Incorporated) and Dennis Johnson (Veterinary Services Team, ECBC) for their support in caring for and handling the animals used in this study and for quality assurance assistance.

QUALITY ASSURANCE

This study, conducted as described in Protocol 99-325, was examined for compliance with Good Laboratory Practices as published by the U.S. Food and Drug Administration in 21 CFR Part 58 (effective 3 Jul 91). The dates of all inspections and the dates the results of those inspections were reported to the Study Director and management were as follows:

Phase Inspected	Date	Reported
Study parameters and exposure	22 May 02	22 May 02
Data and Final Report	26 Jul 04	26 Jul 04

To the best of my knowledge, the methods described were the methods followed during the study. The report was determined to be an accurate reflection of the raw data obtained.

DENNIS W. JOHNSON
Quality Assurance Coordinator
Toxicology, Aerosol Sciences and Obscurants Senior Team
Research and Technology Dir.

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LOW-LEVEL CYCLOSARIN (GF) VAPOR EXPOSURE IN RATS: EFFECT OF EXPOSURE CONCENTRATION AND DURATION ON PUPIL SIZE

1. INTRODUCTION

Acute low-level exposure to cyclosarin (GF) vapor results in both systemic and local toxic effects, which are mediated primarily via inhalation and ocular routes, respectively. The first eye sign to appear following whole-body exposure to low dose nerve agent vapor is miosis, which may be accompanied by a sensation of dimness of vision. With increasing doses in humans, this may be accompanied by ciliary spasm, headache, and eye pain (Sidell, 1992). In estimating the biological impact of GF vapor exposure on the eye, it is necessary to quantitatively relate the probability of eye responses, such as miosis, to exposure parameters. At minimum, these exposure parameters include atmospheric concentration (C) and exposure duration or time (t). The difficulty in using Ct to compare data from different studies is the traditional assumption that integration of vapor concentration over time (Ct or dosage) for any biological effect is constant (Haber's rule; Haber, 1924). Previously, it was reported that the relationship between exposure concentration-time and lethal response in rats exposed to GB (sarin) vapor (Mioduszewski et al., 2001; 2002b) could not be adequately described by Haber's rule. The objective of the present study was two-fold: a) to determine the EC_{50} for GF vapor-induced miosis and associated probit slope in the rat and b) to model the relationship between GF vapor exposure concentration (C), duration of exposure (t), and the probability of miosis. This study examined the relationship between exposure concentration and miosis in rats exposed to GF vapor for 10, 60, or 240 min. Portions of this study were presented earlier (Whalley et al., 2002; 2003).

Very little is published in the open literature regarding the inhalation effects of GF. Even less is published on the low-level inhalation effects of this nerve agent. Following World War II, GF, originally synthesized by the Germans, was a compound of interest because it appeared to possess percutaneous toxicity that other G-agents lacked. Much of the information on the *in vivo* toxic effects of GF by various routes of administration in a number of different species was reported in the 20th Century by the military literature of the late forties and early fifties; however, although the material is unclassified, the distribution still remains limited for most of the publications. Cresthull et al. (1957) studied incapacitation and lethality in rhesus monkeys (mostly females, but the exact breakout of sexes was not given in the report) exposed to GA, GB or GF vapors. For each agent the LCt_{50} values were significantly lower for a 2 min exposure than for a 10 min exposure. For example, the 2 min LCt_{50} value for GF was 75 mg.min/m^3 while the 10 min LCt_{50} value was 130 mg.min/m^3 (in both cases the slope was 11.0). For GB, the 2 min and 10 min LCt_{50}s were 42 (slope was 3.4; however, the authors believed this slope should have been parallel with the 10 min exposure) and 74 (slope was 11.0), respectively. A 20 m^3 dynamic flow chamber was used for the 10 min GF exposures (and all the GA and GB exposures), while a smaller 4.3 m^3 chamber was used for the 2 min GF exposures. In this report (Cresthull et al., 1957), it was pointed out that GF vapor was more toxic than GB vapor in exposed mice and rats but that GB vapor was more toxic than GF vapor in monkeys.

Most of the open modern literature that is available utilizes parenteral administration of this nerve agent to study the inhibition, reactivation and aging kinetics of GF-inhibited human cholinesterases (Worek et al., 1998); the evaluation of the acute toxicity, pathology and treatment of GF poisoned male rhesus monkeys (Koplovitz et al., 1992; Young and Koplovitz, 1995); and the acute toxicity and the evaluation of pretreatment and treatment therapy following GF poisoning in mice and guinea pigs (Koplovitz et al., 1996). It was believed (Sidell, 1997; Dunn et al., 1997) that Iraq switched from the manufacture of GB to the manufacture of GF when GB precursors, but not GF precursors, were banned during the first Persian Gulf War (1990-1991). No previous study was found that dealt with the miosis effects of low level or non-lethal concentrations of GF. However, very recently, a report (Anthony et al., 2003) was published on the inhalation toxicity of GF vapor in rats as a function of exposure concentration and duration. This report also compared the potency of GF to GB.

2. OBJECTIVES

Determine the exposure conditions for GF vapor-induced miosis in rats: a) EC_{50} (miosis) for 10, 60, and 240 min exposures and b) examine potential male vs. female differences.

Is Ct constant over time for miosis? If not, what model best describes the relative influence of exposure concentration (C) and duration (t) on the probability of miosis.

3. MATERIALS AND METHODS

3.1 Chemicals.

Cyclohexyl methylphosphonofluoridate (GF or cyclosarin, also known as EA 1212; see Appendix B for more synonyms) was used for all vapor exposures in this study. GF (lot # GF-93-0034-109 (GF-S-6092-CTF-N-1)) was distilled by ECBC's Advanced Chemistry Team and verified as 98.87 ± 0.50 wt. % pure (as determined by quantitative ^{31}P NMR) and stored in sealed ampoules containing nitrogen (note: this agent was not chemical agent standard analytical reagent material (CASARM)-grade). Ampoules were opened as needed to prepare external standards or to be used as neat agent for vapor dissemination. All external standards for GF vapor quantification were prepared on a daily basis. Triethylphosphate (TEP, 99.9% purity), obtained from Aldrich Chemicals, Milwaukee, WI, was used as the internal standard for the GF purity assay.

Prior to distillation, analysis for GF impurities of GF-S-6092-CTF-N-1 was conducted using ^{1}H, ^{13}C and ^{31}P NMR. Acid-base titration showed the following impurity percentages based on mole ratios:

Compound	Mole %	Calculated Wt %
GF	96.5	96.6
Methylphosphonicdifluoride (DF)	0.5	0.3
Methylphosphonofluoridic acid	0.5	0.3
Dicyclohexyl methylphosphonate	1.5	2.1
Hexyl methylphosphonofluoridate	0.1	0.1
Diisopropylurea	0.5	0.4
Cyclohexanol	0.1	0.1
Hexanol	0.1	0.06
Ethanol	0.1	0.02
Methyl methylphosphonofluoridate	0.05	0.03
Dimethylphosphinic fluoride	0.02	0.01
Cyclohexyl dimethylphosphinate	0.01	0.01

3.2 Vapor Generation.

By directing the nitrogen carrier gas through a glass vessel (multi-pass saturator cell) containing liquid GF (Figure 1), saturated GF vapor streams were generated. The saturator cell consisted of a 100-mm long, 25-mm o.d. cylindrical glass tube with two (an inlet and an outlet) vertical 7-mm o.d. tubes connected at each end. The main body of the saturator cell contained a hollow ceramic cylinder that served to increase the contact area between the liquid GF and the nitrogen. The saturator cell was fabricated to allow nitrogen to make three passes along the surface of the wetted ceramic cylinder before exiting the outlet arm of the glass cell. The saturator cell body was also immersed in a constant temperature bath so that a combination of nitrogen flow and temperature could regulate the amount of GF vapor going into the inhalation chamber. This entire apparatus was contained within a generator box mounted at the top of the inhalation chamber.

Typically, the saturator cell was loaded with 2-3 mL of liquid GF (non-CASARM grade). Immediately after loading, a low nitrogen flow rate (1-2 mL/min) continuously flowed through the cell to maintain the integrity of the liquid GF. This allowed the saturator cell to be used as a generation source for approximately 1-2 weeks.

In this study, the GF vapor concentration in the chamber ranged from 0.0036 to 0.465 mg/m^3. Generation and chamber parameters to achieve this range corresponded to a nitrogen generator flow rate of 1-13 mL/min with a water bath temperature of 15-16 ^oC and a chamber flow of 1,600 – 1,700 L/min.

3.3 Inhalation Chamber.

Whole-body exposures were conducted in a 750 L dynamic airflow inhalation chamber (Figure 1). The Rochester style chamber was constructed of stainless steel with Plexiglas windows on each of its six sides. The interior of the exposure chamber was maintained under negative pressure (0.50" H_2O), which was monitored with a calibrated magnehelix (Dwyer, Michigan City, IN). A thermoanemometer (Model 8565, Alnor, Skokie, IL) was used to monitor chamber airflow at the chamber outlet.

3.4 Vapor Sampling/Analysis.

Two sampling methods were used to monitor and analyze the GF vapor concentration in the exposure chamber. The first method was a quantitative technique using solid sorbent tubes (Tenax) to trap GF vapor, followed by thermal desorption and gas chromatographic (GC) analysis (HP Model 6890, Agilent Technology, Baltimore, MD). The second method was a continuous monitoring technique using a phosphorus monitor (HYFED, Model PH262, Columbia Scientific, Austin, TX). Output from the HYFED provided a continuous strip chart record of the rise, equilibrium, and decay of the chamber vapor concentration during an exposure.

All samples were drawn from the same area (middle) of the chamber. Solid sorbent tube samples were drawn after the chamber attained equilibrium (defined as 99% of the target concentration for the run) while the HYFED monitored the entire run. Solid sorbent tube samples were drawn from the chamber approximately every 10 min with each sample draw lasting 1-8 min depending upon chamber concentration and duration of exposure. All sample flow rates for the solid sorbent tube systems were controlled with calibrated mass flow controllers (Matheson Gas Products, Montgomeryville, PA). Typical flow rates were 400 sccm (standard cubic centimeters per min) for the sorbent tubes. Flow rates were verified before and after sampling by temporarily connecting a calibrated flow meter (DryCal®, Bios International, Pompton Plains, NJ) in-line to the sample stream.

3.5 Solid Sorbent Tube System.

The automated solid sorbent tube sampling system consisted of four parts: (1) a heated sample transfer line (2) heated external switching valve (3) thermal desorption unit and (4) gas chromatograph. A stainless steel sample line (1/16" o.d. x 0.004" i.d. x 6' length) extended from the middle of the chamber to an external sample valve. The sample line was commercially treated with a silica coating (Silicasteel® Restek, Bellefonte, PA) and covered with a heated (200 °C) sample transfer line (Unique Products, Hazel Park, MI). The combination line coating and heating minimized GF absorption onto sample surfaces. From the transfer line, the sample entered a heated (160 °C) 6-port gas-switching valve (UWP, Valco Instruments, Houston, TX). In the by-pass mode, GF vapor from the chamber continuously purged through the sample line and out to a charcoal filter. In the sample mode, the gas sample valve redirected GF vapors from the sample line to a Tenax TA sorbent tube (60-80 mesh) located in the thermal desorption unit (ACEM-900, Dynatherm Analytical Instruments, Kelton, PA). Temperature and flow programming within the Dynatherm was used to desorb GF from the sorbent tube directly onto the GC column (RTX-5, 30 m, 0.32 mm i.d., 1 mm thickness); this was followed by flame photometric detection (FPD - phosphorus mode).

The solid sorbent tube sampling system was calibrated by direct injection of external standards (GF/hexane - µg/mL) into the heated sample line of the Dynatherm. In this way, injected GF standards were put through the same sampling and analysis stream as the chamber samples. A linear regression fit ($r^2 = 0.999$) of the standard data was used to compute for the GF concentration of each chamber sample. The GF exposure concentration represented the mean value of all the sorbent tube samples taken for each exposure.

3.6 Animal Exposures.

Young adult male and female Sprague-Dawley rats (8 to 10 weeks) were purchased from Charles River Laboratories, Inc., Wilmington, MA. Rats were identified by tail tattoo and housed individually in plastic shoebox cages in an Association for Assessment and Accreditation of Laboratory Animal Care International (AAALAC) accredited facility. Ambient holding conditions were maintained at 21 ± 3 °C, 40 - 70% relative humidity (RH), and a 12:12 hr (light: dark) cycle. Rats were provided with certified laboratory rat chow and water ad libitum (automatic watering system using a reverse osmosis process), except during vapor exposure. Animals were quarantined for at least 5 days prior to exposure.

3.6.1 Whole-Body Inhalation Exposures.

All animals were exposed (whole-body) to GF vapor in a 750-L dynamic airflow inhalation chamber. Rats were exposed to a fixed concentration of GF vapor for a fixed duration (10, 60 or 240 min), and observed for clinical signs for up to seven days post-exposure. In most exposures, groups of 10 male (M) rats and 10 female (F) rats were exposed in the chamber. However, in some instances male and female rats were exposed separately. The rats of an exposure group were placed in stainless steel compartmentalized cages (20"w x 14"l x 4" h) with each rat in a separate compartment. Also, 5 male and 5 female rats (control animals) were exposed to air only in a separate 750-L dynamic airflow inhalation chamber. Same gender rats were arranged in alternating diagonals within the cage (Mioduszewski et al., 2001; 2002a and 2002b; Anthony et al., 2003). Physical parameters monitored during exposure included chamber airflow (monitored continuously), as well as chamber room temperature and relative humidity. During inhalation chamber operations, the airflow through the chamber was kept constant. Exposure duration was defined as the interval from the start of the flow of agent into the chamber to the time-point when the agent supply is stopped (MacFarland, 1987). The time required for the vapor concentration to reach 99% of its equilibrium value is denoted as t_{99}. An equal amount of time is required for the chamber to lose 99% of its equilibrium concentration after the agent supply is stopped. Immediately after completion of the exposure period, the chamber was purged with air for a minimum time of t_{99}. Control rats were exposed to air in a separate chamber that was identical in construction to the agent chamber, but was never used for agent exposures.

The T_{99} values for chamber saturation ranged from 5.7 min to 6.8 min for the various exposure groups (see Appendix C for the T_{99} values for each exposure group).

3.6.2 Blood Sample Collection.

Three blood samples were collected (within 24 hr prior to exposure, within 60 min following exposure, and at the time of euthanasia, 7 days post-exposure) from each rat for the purpose of measuring carboxylesterase activity and cholinesterase activity in both red blood cell and plasma components. Blood samples were collected from the tail vein (at 24 hr prior to exposure and within 60 min following exposure) and the heart (post-mortem) into glass tubes containing ethylene diamino tetraacetic acid (EDTA). Personnel at the Edgewood Chemical Biological Center (ECBC), APG, MD, using a modification of the Ellman reference

method (Ellman et al., 1961), performed assays of red blood cell acetyl cholinesterase (AChE), plasma butyrylcholinesterase (BuChE), and carboxylesterase (CaE) activity.

3.6.3 GF Regeneration.

Sample collection for GF regeneration was performed as follows (Jakubowski et al., 2002 and 2003). Whole blood from the GF exposed male and female rats was collected in capped polyethylene tubes that contained a drop of EDTA from the tail vein before and after inhalation exposure. Cardiac puncture was utilized for the final blood collection after death. The samples were centrifuged at 15000 rpm for 3 min. The resulting red blood cell pack and serum/plasma samples were analyzed for regenerated agent by the addition of acetate buffer and fluoride ion.

The samples were prepared as follows (Jakubowski et al., 2002 and 2003). To weighed samples (0.1-0.5 g), 1.5 mL of acetate buffer (pH 3.5) and a prescribed amount of 6 M potassium fluoride (KF) solution was added to plasma (0.02 mL) or to packed blood cells (0.2 mL) and vortexed. The RBC containing samples were centrifuged at 15000 rpm for 3 min. The liquid portion of each sample was transferred to a conditioned C18 SPE cartridge (200 mg; Waters Associates, Millipore Corporation, Milford, PA). The SPE cartridges were conditioned with 1 mL ethyl acetate, followed with 1 mL isopropanol and finally with 1 mL acetate buffer. The sample was eluted with 1 mL ethyl acetate over sodium sulfate. The final preparation of the samples was as follows: First spike 0.002-0.200 mL of the ethyl acetate extract in a DAAMS sorbent tube (Tenax-TA); then spike the tube with internal standard (400 pg of $^{2}H_{10}$-DEEP, decadeuterated diethyl ethylphosphonate, or $^{2}H_{11}$-GF, which were synthesized at ECBC) and finally flush the tube with N_2 for 3-6 min at a flow rate of 75 cc/min.

The regenerated GF (R-GF) was analyzed as follows (Jakubowski et al., 2002 and 2003). The sample was introduced into a Dynatherm ACEM 900 (Dynatherm Inc., Kelton, PA) tube set at 200 °C/3 min (the trap was 265 °C/3 min; the valve was 230 °C; and the interface was 250 °C). The GC column used was a DB5 (30 m x 0.25 mm x 0.5 m film). The GC oven program was as follows: initial temperature was 35 °C for 3 min to 140 °C @15 °C/min (0 min hold) to 265 °C @ 50 °C/min (2.3 min hold). The DAAMS tube was reconditioned at 275 °C for 4-6 min. The R-GF was detected by either dual flame photometric detectors or by mass spectrometry (Model 6973 MSD Agilent, Avondale, PA).

3.6.4 Assessing Pupil Diameter.

This study utilized a novel non-invasive system whereby projected infrared (IR) light (880 nm) reflects off the animal's retina back through the pupil producing an image of a bright pupil surrounded by a dark iris (Miller et al., 2002, 2003a and 2003b). Previous studies in this laboratory utilized the Lennox method (Lennox, 1969) to measure pupil diameters and miosis in rats (Anthony et al., 2003; Mioduszewski et al., 2001; 2002a; 2002b). In this study the pupil and iris of the right eye of control and exposed animals were assessed. Data were collected under low light conditions (1 foot-candle). The pupil image is very distinct in a normal or a dilated pupil but dims as the pupil contacts (Figure 2 shows rat eye images made using normal and IR lighting). Labview and IMAQ (National Instruments, Austin, TX) software was used to

write the novel image analysis program. National Instruments also produced the image acquisition computer card (PCI-1411). Data Science Automation (Canonsburg, PA) supplied the Sony CCD black and white video camera (XC-ST50), the video camera power supply (CD700), the 75 mm F2.7 video camera lens (LMV7527), the tripod adapter (VCT-ST701) and the 100 candle IR spotlights (SL2420-880100XL24VOLT).

The automated acquisition and analysis program performed three functions (Miller et al., 2002 and 2003a). The first function was to capture a still image from a live streaming video image and save it as a JPG image file using the animal number and the image number to create a unique file name. This image is not altered but is saved in raw form. The second function filters a copy of the image to isolate the pupil from the remainder of the image and to measure the pupil area. The third function is to time-stamp and to transfer image information, such as pupil size and animal number, to a spreadsheet.

3.7 Data Analysis.

Statistical analysis routines, including Bliss probit analysis (Bliss, 1934, 1935, 1937, 1952), Mann-Whitney Rank Sum test, Wilcoxon Signed Rank test, analysis of variance, and regression analysis, contained within Minitab®, Version 13 (Minitab, Inc., State College PA), were used for the analysis of the data (Minitab, 2002).

4. RESULTS

4.1 Pupil Response.

The first image of Figure 3 shows a typical pupil response as measured by the IR camera under low light conditions prior to GF exposure. The next IR image shows the miotic response measured an hour following a GF exposure and the subsequent IR images show the recovery of pupil response with time. Figures 4-6 show the average pupil diameter pre-exposure (expressed as a percent of pre-exposure pupil diameter), within 1 hr post-exposure, and at 1, 2, and 7 days post-exposure for exposed and control rats by gender. A rat was classified as having miosis if its pupil diameter, measured approximately 30 min after exposure, was half or less of its pre-exposure pupil diameter (Mioduszewski et al., 2001; 2002a; 2002b). The pre-exposure pupil diameter was the geometric mean of several pre-exposure pupil diameter measurements of the rat. By this definition of miosis, none of the 120 control rats (male and female) developed miosis after exposure to air. Table 1 gives the fraction of female and male rats in each GF-exposed group that developed miosis.

Figures 7-12 show the ratio (post-exposure pupil diameter)/(pre-exposure pupil diameter) divided by the geometric mean post/pre pupil diameter of matched air-exposed control rats plotted against the exposure concentration for each exposure duration and gender of rat. Also shown in these figures are the dose-response curves fit separately to each gender-exposure duration group. When overlaid, the dose-response curves for 60-min and 240-min exposure durations cross; hence, at some concentration, the curves indicate more pupil shrinkage for a

60-min exposure than for a 240-min exposure. Therefore, when probit analysis was done, the probit slope was required to be the same at all three exposure durations. Probit analysis results can be found in Table 2 and details of the analysis are in Appendix A, including estimates of EC_{50}'s, ECT_{50}'s, 95% fiducial intervals, and probit slope.

4.2 Gender Differences in the Effect of Cyclosarin (GF) Vapor on Miosis.

The difference between male and female rats was statistically significant for all three exposure durations ($p < 0.05$), with the EC_{50} values for female rats being lower than the EC_{50} values for male rats at all three exposure durations. The EC_{50} for male rats was approximately twice the EC_{50} for female rats. The ratio of male to female rat EC_{50} decreased with exposure duration, but this trend was not statistically significant. This trend is opposite to that reported by Mioduszewski et al. (2002a, 2003) where the ratio of male to female rat EC_{50} increased with exposure duration; however, this trend was also not statistically significant.

4.3 A Toxic Load Model for the Probability of Miosis.

Using data on all exposed rats (239 rats, of which 103 had miosis) yielded the following model describing the relationship between probability of miosis and exposure conditions; sex is coded –1 for female rats and 1 for male rats. The standard error (SE) of each coefficient is listed below the coefficient.

$$\begin{array}{l} \text{Normit}^{1} = 1.9706 + 4.1088\ \log(C) + 2.0759\ \log(T) - 0.68619\ \text{Sex} \\ \quad\quad\quad\quad \text{SE:}\ \ 0.2801 \quad\ 0.3394 \quad\quad\quad 0.2486 \quad\quad\ 0.08888 \end{array} \qquad (1)$$

All model terms[2] in Equation [1] are highly significant ($p < .001$). The toxic load exponent is 1.98, with an approximate standard error of 0.14 {from the propagation of error formula (Barry, 1978):

$$SE(A/B) = (A/B)[\text{variance}(A)/A^2 + \text{variance}(B)/B^2 - 2\cdot\text{covariance}(A,B)/(A\cdot B)]^{(1/2)}\}.$$

Equation (1) determines the combinations of exposure concentration and duration (on the right hand side of the equation) that produce the fraction of rats (on the left hand side) with at least 50% pupil shrinkage.

The fitted model in Equation (1) was obtained from the use of an ordinal regression analysis of pupil size on Log(C), Log(T), and sex using MINITAB®. Sommerville (2002, 2003) previously used ordinal regression for the analysis of G agent lethality and severe effect data. Pupil size was categorized into four classes:

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[1] Normit is the Z transform (the inverse cumulative distribution function of the standard normal distribution) of the fraction of rats with miosis.

[2] All logarithms in this report are base 10 logarithms; concentrations are given in mg/m^3 and exposure durations in minutes.

Pupil Size	Ordinal Class
0.842 - 1.30	3
0.501 - 0.841	2
0.160 - 0.500	1
0.00 - 0.159	0

Pupil size is the ratio of post-exposure pupil diameter divided by the pre-exposure pupil diameter, and adjusted for the control rats by dividing by the geometric mean of the same ratio for the control rats of the same sex associated with the exposure group. The ordinal classes 0 and 1 correspond to miosis. Thus the ordinal regression with a normit link function generates the model in Equation (1) and additional intercepts for other ordinal class boundaries.

Our model is that a Z transform of pupil size will be a straight-line function of Log(C) and of Log(T), but random variation makes pupil size exceed 1 so that a Z transform cannot be done. Mioduszewski et al. (2002a) used group averages of pupil size to avoid the problem of pupil sizes greater than one. The ordinal regression approach also avoids the problem of pupil sizes greater than one and allows one analysis to generate both a model for probability of miosis and a model for pupil size.

4.4 A Toxic Load Model for Pupil Diameter.

Because the boundaries for the classes in the ordinal regression were chosen to correspond to Z values of -1, 0, and 1 for pupil size (see the ordinal table above), the difference between the constants for the boundaries corresponding to Z values of -1 and 1 in the ordinal regression corresponds to 2 units of Z(pupil size). The constant for Z(pupil size) = 1 was 0.1696 and the constant for Z(pupil size) = –1 was 3.5627, so 0.1696 – 3.5627 = – 3.3931 normits of percent rats with miosis equals two Z-units of pupil size. Therefore, –3.3931 / 2 = –1.6966 normits of percent of rats with miosis equals one Z-unit of pupil size. The model for the pupil size of the median rat is:

$$Z(\text{pupil size}) = -1.1615 - 2.4218 \cdot \text{Log}(C) - 1.2236 \cdot \text{Log}(T) + 0.40445 \cdot \text{Sex} \qquad (2)$$

The coefficients in this model are the coefficients from the model for percent of rats with miosis divided by –1.6966. The sign of the coefficients changes because pupil size and miosis are defined in opposite directions (small pupils indicate miosis).

Alternatively, we can develop a model for pupil shrinkage instead of pupil size. Pupil shrinkage is defined as 1–(post/pre pupil diameter ratio). Therefore Z(pupil shrinkage) =–Z (pupil size), and we obtain the model for pupil shrinkage of the median rat by multiplying the coefficients of the model for pupil size of the median rat by –1. The model for pupil shrinkage of the median rat is:

$$Z(\text{pupil shrinkage}) = 1.1615 + 2.4218 \cdot \text{Log}(C) + 1.2236 \cdot \text{Log}(T) - 0.40445 \cdot \text{Sex} \qquad (3)$$

Figures 13 and 14 illustrate these toxic load models.

Within the range of the data, equation [3] can be used to find the EC50 for any definition of miosis. For example, to find the EC50 for 70% pupil shrinkage (that is, a pupil diameter 30% of pre-exposure size) after a 1-hr exposure, substitute Z(0.7) for the left hand side of equation (3), use T = 60 min and Sex = 1 or –1, and solve for Log(C), which is the logarithm of the EC50. Equation (3) determines the combinations of exposure concentration and duration (on the right hand side of the equation) that produce the definition of miosis (on the left hand side) in 50% of exposed rats.

4.5 Blood Esterase Activities.

Red blood cell acetylcholinesterase (AChE) activity was inhibited, while plasma butyrylcholinesterase (BuChE), and carboxylesterase (CaE) activities were slightly increased as a result of exposure to various combinations of GF vapor concentration and exposure duration (see Figures 15-20, where control rats are arbitrarily plotted at CT = 0.5 to fit on the log scale for CT). Each rat's AChE, BuChE, and CaE activity at 1 hr post-exposure was divided by its pretreatment value collected at 24 hr prior to exposure. Median pretreatment levels of BuChE activity were higher ($P < 0.001$) in female (1037.5 U/mL) than in male rats (328 U/mL), as determined by the Mann-Whitney Rank Sum test. The BuChE results are similar to those found in other reports (Mioduszewski et al., 2002 and 2003). The gender difference was reversed for pretreatment AChE activity, with male rats having a significantly ($P < 0.001$) higher median activity (1.11 U/mL) than female rats (0.79 U/mL), as determined by the Mann-Whitney Rank Sum test. No difference was noted between pretreatment male (2.46 μM) and female (2.61 μM) median CaE activity. Other studies have reported somewhat different pretreatment gender differences in AChE and CaE activities (Mioduszewski et al., 2002a, 2002b and 2003). At 1 hr after exposure, the median post-/pre-exposure activity ratio of exposed rats was less than 1 for AChE but greater than 1 for both BuChE and CaE ($p < 0.001$ by the Wilcoxon Signed Rank test). For AChE and CaE, there was no difference between the medians of exposed and control rats (as determined by the Mann-Whitney Rank Sum test). For BuChE, however, the increase in activity was 31% for control rats and 15% for exposed rats; the difference in the increase in activity between control rats and exposed rats was statistically significant ($p = 0.03$). At seven days post-exposure, there was no statistically significant difference in esterase activity values between exposed and their respective control rats.

4.6 GF Regeneration.

Full details of the possible relationship between regenerated GF (R-GF) and GF-induced miosis will be reported in another publication (Jakubowski, et al., 2004). GF was regenerated from blood samples of vapor-exposed rats by the addition of fluoride ion at pH 4 and the samples were analyzed by GC-FPD and GC-MS. Levels of R-GF in the red blood cell (RBC) fraction of the samples were five to 40 times lower than in plasma (Figure 21). All controls were negative for R-GF.

5. DISCUSSION

The curves of GF-induced miosis (present study) and GF inhalation lethality (Anthony et al., 2003) in rats are shown in Figure 22. There is at least two orders of magnitude differences between the curves. A similar difference was also found between GB-induced miosis (Mioduszewski et al., 2002a) and GB inhalation lethality (Mioduszewski et al., 2001) in rats.

The toxic load exponents for GF- and GB-induced miosis in rats are 1.98 (present study) and 1.96 (Mioduszewski et al., 2002a), respectively. This suggests that there may be no difference among the G-agents in terms of the time dependence of G-agent induced miosis in rats.

The toxic load exponents for GF and GB lethality in rats are 1.27 (Anthony et al., 2003) and 1.66 (Mioduszewski et al., 2001), respectively. Both of these values are less than what were observed from the corresponding miosis toxic load exponents for these two agents. This suggests that G-agent induced miosis in rats is more sensitive to changes in exposure duration than lethality (for exposure durations less than 360 min).

No mydriasis was observed in the present study; however, Anthony et al. (2003) observed mydriasis in his rat GF lethality study. This is probably due to the major differences in the range of GF vapor dosages used in the two studies. The lowest dosage (Ct) used in Anthony et al. (2003) was 172 mg-min/m^3, whereas the highest Ct used in the present study was only 10.1 mg-min/m^3. Thus, high dosages of GF vapor are necessary in order to induce mydriasis in rats via whole-body exposures.

In the present study, female rats were found to be more sensitive to GF-induced miosis than male rats. The same gender sensitivity results have been recently reported for several other CW agent-endpoint combinations in rats: GF inhalation lethality (Anthony et al., 2003); GB inhalation lethality (Mioduszewski et al., 2001); and GB-induced miosis (Mioduszewski et al., 2002a and 2003).

6. SUMMARY AND CONCLUSIONS

The probability of cyclosarin (GF) vapor-induced miosis (defined as a post-exposure pupil diameter 50% or less of the pre-exposure pupil diameter) was estimated in rats exposed to various combinations of exposure concentration and duration. Groups of male and female Sprague-Dawley rats were exposed to GF vapor for a single duration (10, 60 or 240 min) in a whole-body dynamic chamber. Pupil diameter was measured by an infrared camera technique. For the six combinations of gender and exposure duration, the effective concentration for miosis in 50% of the exposed population (EC_{50}) and the common probit slope were determined. Contrary to Haber's rule, ECt_{50} values increased with exposure duration (i.e., the Ct for 50% of the exposed population to show miosis was not constant over time). Female rats were more sensitive to GF vapor toxicity than male rats. Miosis was the only clinical sign noted following GF vapor exposure. Mydriasis was not observed in the present study. Depression of

blood esterase (acetylcholinesterase, butyrylcholinesterase and carboxylesterase) activities due to low-level range of GF vapor concentrations was also investigated. GF was regenerated from blood samples of vapor-exposed rats by the addition of fluoride ion at pH 4 and the samples were analyzed by GC-FPD and GC-MS. Levels of regenerated GF in the red blood cell (RBC) fraction of the samples were five to 40 times lower than in plasma. All controls were negative for regenerated GF.

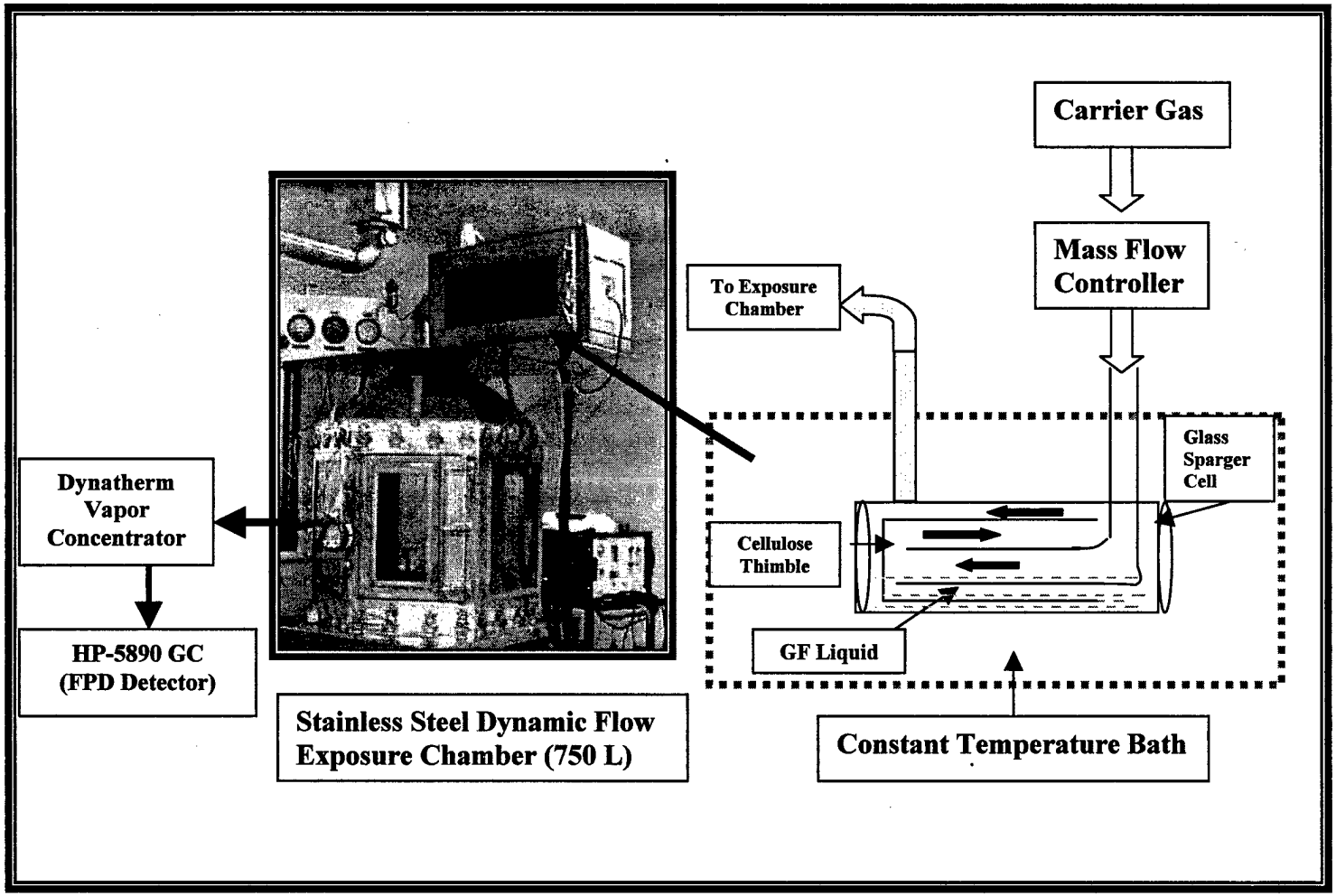

Figure 1. Cyclosarin (GF) Vapor Generation, Chamber Atmosphere Sampling/Analysis/Quantification, and Exposure Chamber

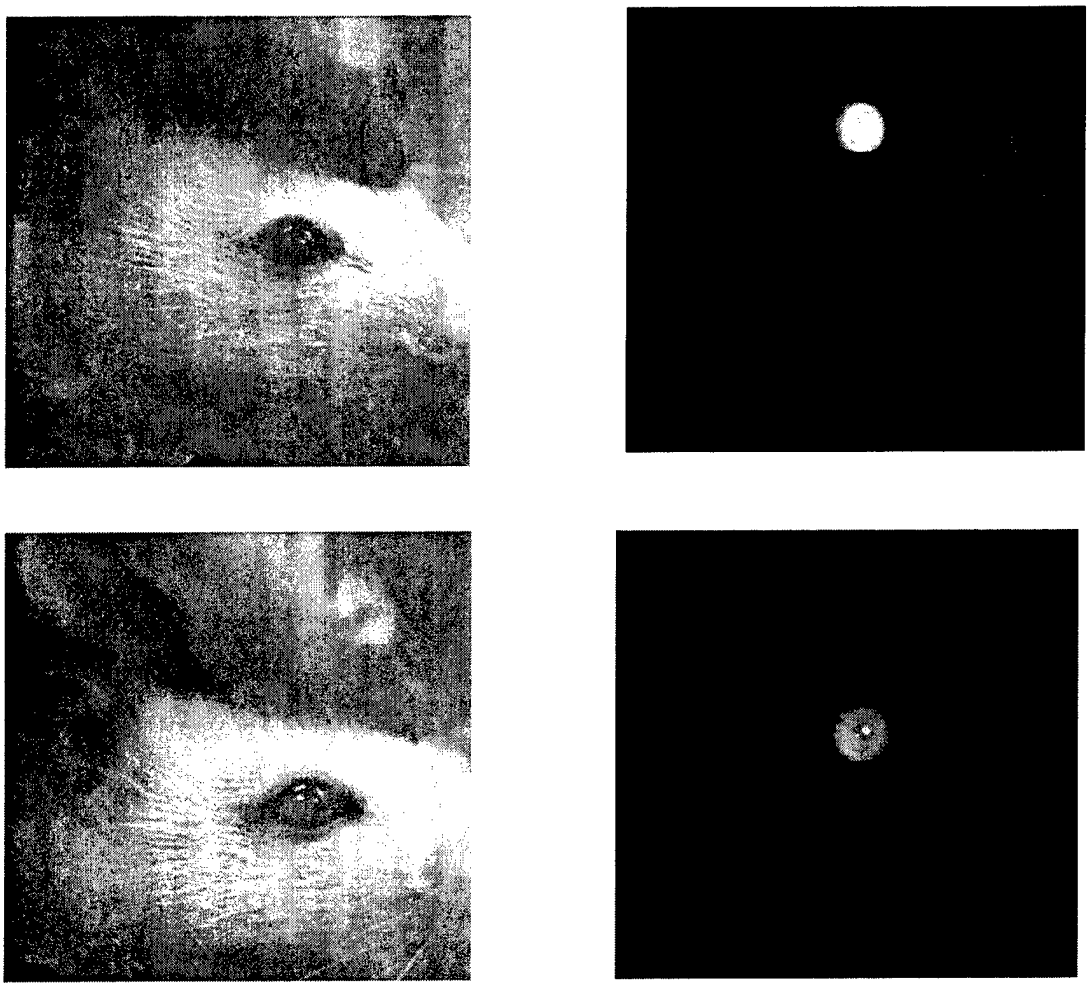

Figure 2. Rat Photographed Using Fluorescent Lighting Under Standard Visible Light Conditions (upper left). Rat IR image without miosis and using fluorescent lighting (lower left). IR image of female rat (#440, Group 15) eye showing a normal response to darkness prior to GF exposure (upper right). IR image of female rat (#440, Group 15) eye showing miosis measured 1 hr after GF exposure (lower right).

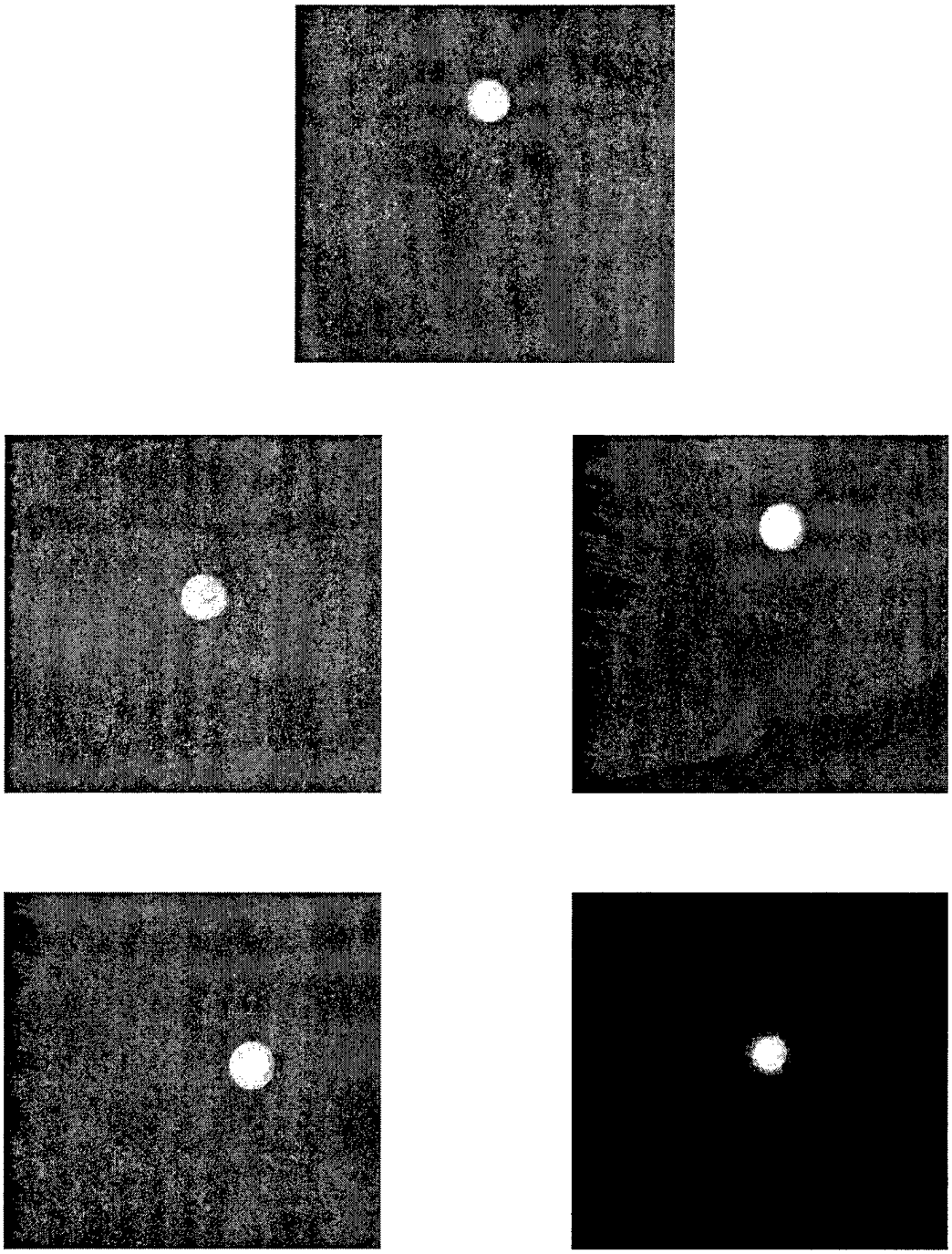

Figure 3. A Typical IR Image of a Female Rat's (rat #440, Group 15) Right Eye Showing the Normal Response to Darkness Prior to GF Exposure (top image). IR image of the same female rat (#440, Group 15) eye showing miosis measured 1 hr after GF exposure, 0.0039 mg/m^3 for 240 min (second row, left image). The subsequent images show the recovery of the same animal's pupil response over time: IR image of pupil 24 hr after GF exposure (third row, left image), 48 hr after GF exposure (second row, right image), and 7 days after GF exposure (third row, right image). All IR images were taken under low light conditions.

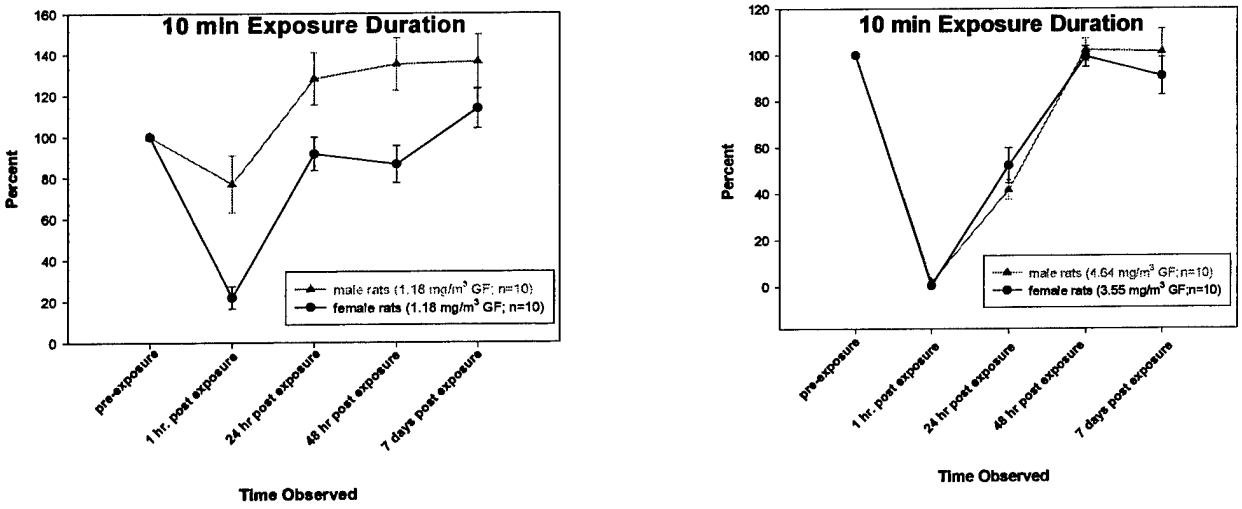

Figure 4. Time Course of 10 min GF Vapor Exposure at Different Concentrations on Pupil Diameter in Male and Female Rats

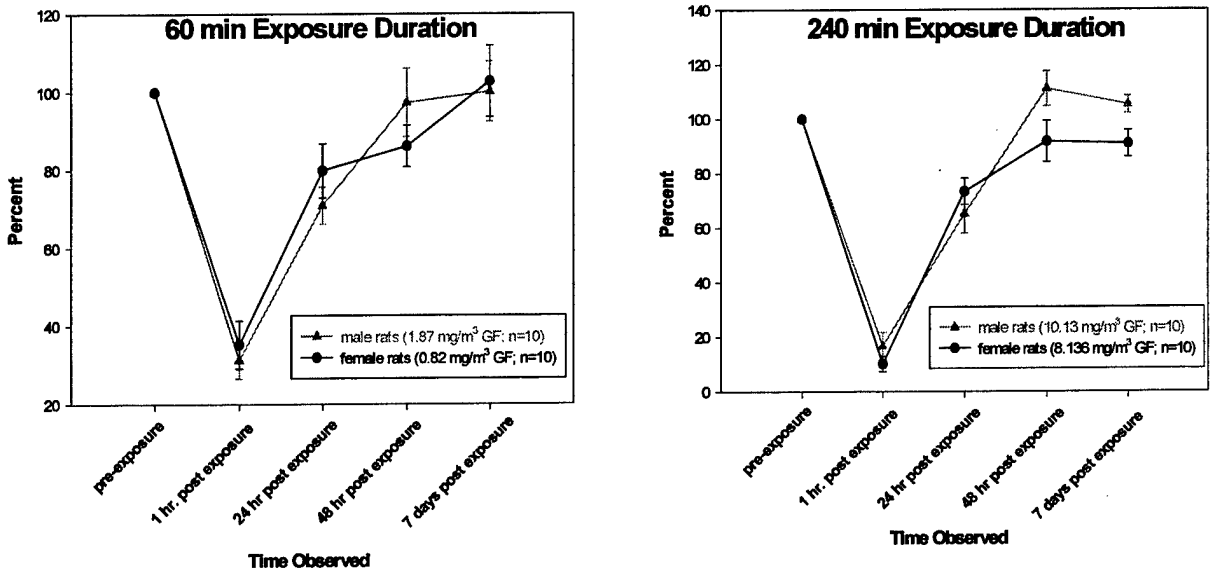

Figure 5. Time Course of 60 and 240 min GF Vapor Exposure on Pupil Diameter in Male and Female Rats

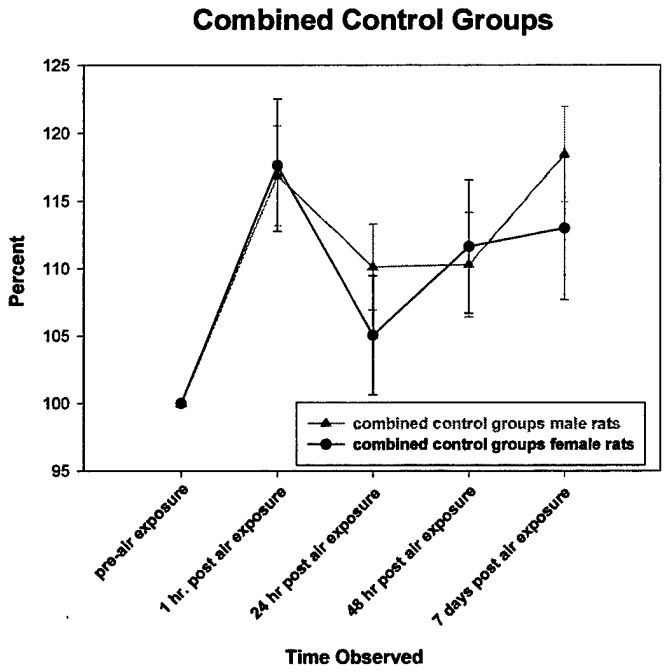

Figure 6. Effects of Air Exposure on Pupil Diameter of Male and Female Rats

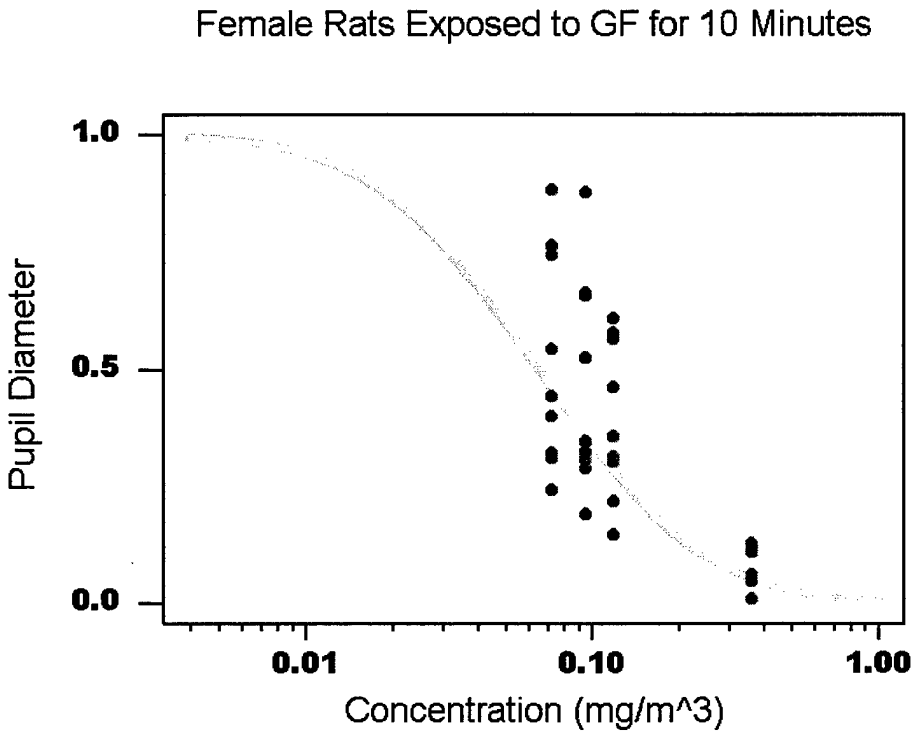

Figure 7. Effects of 10 min GF Vapor Exposure (various fixed concentrations) on Pupil Diameter of Female Rats

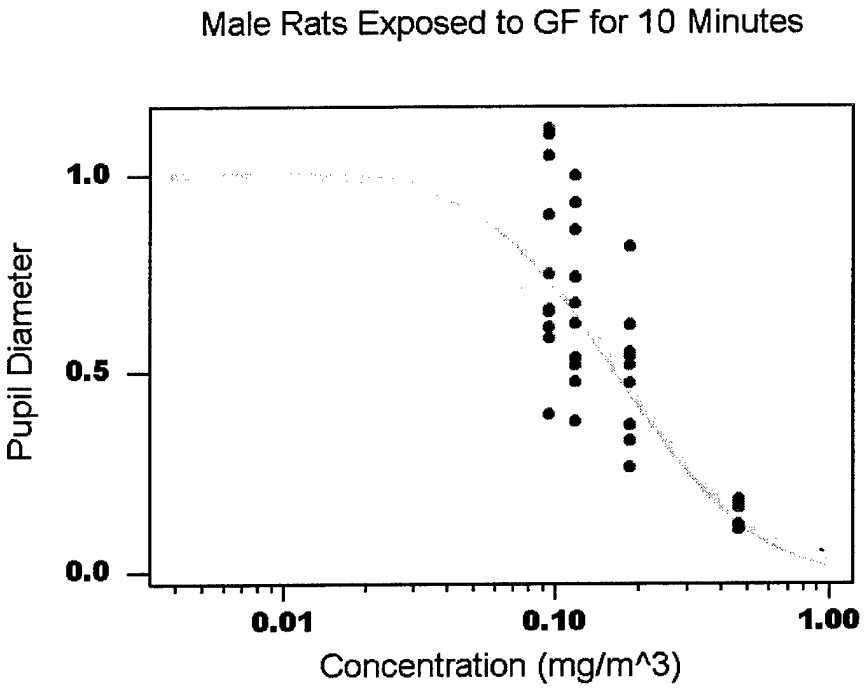

Figure 8. Effects of 10 min GF Vapor Exposure (various fixed concentrations) on Pupil Diameter of Male Rats

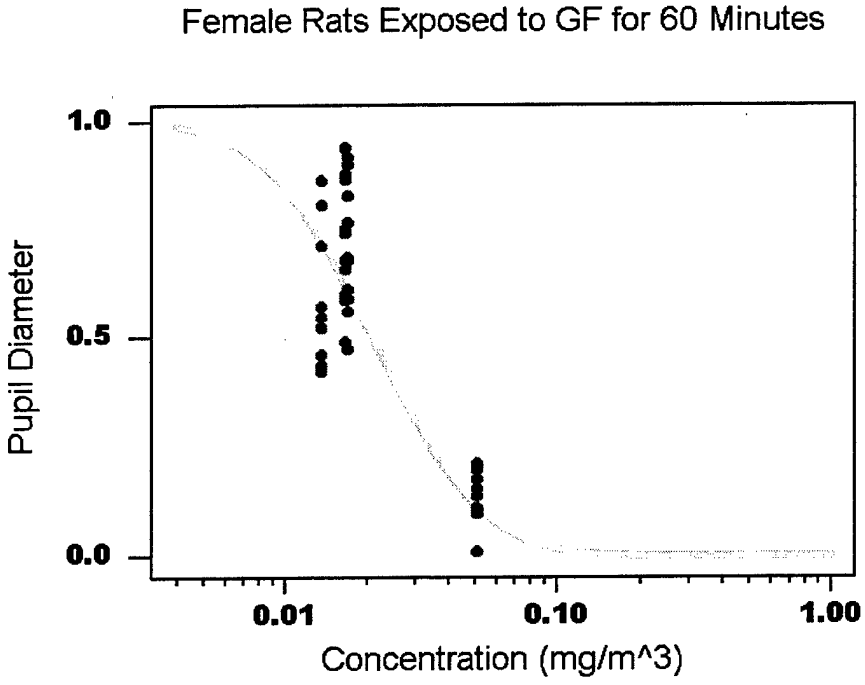

Figure 9. Effects of 60 min GF Vapor Exposure (various fixed concentrations) on Pupil Diameter of Female Rats

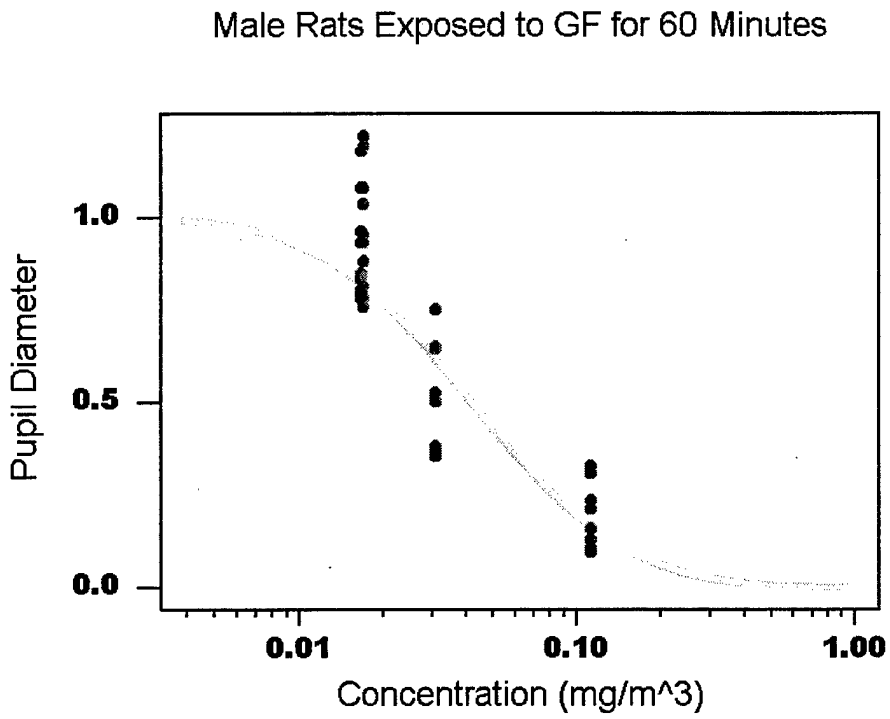

Figure 10. Effects of 60 min GF Vapor Exposure (various fixed concentrations) on Pupil Diameter of Male Rats

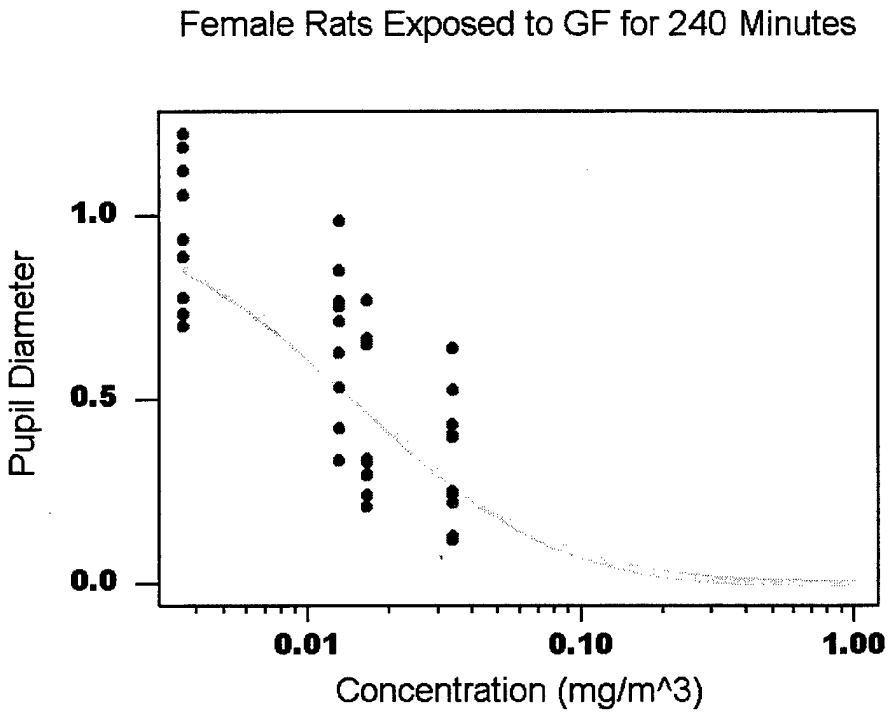

Figure 11. Effects of 240 min GF Vapor Exposure (various fixed concentrations) on Pupil Diameter of Female Rats

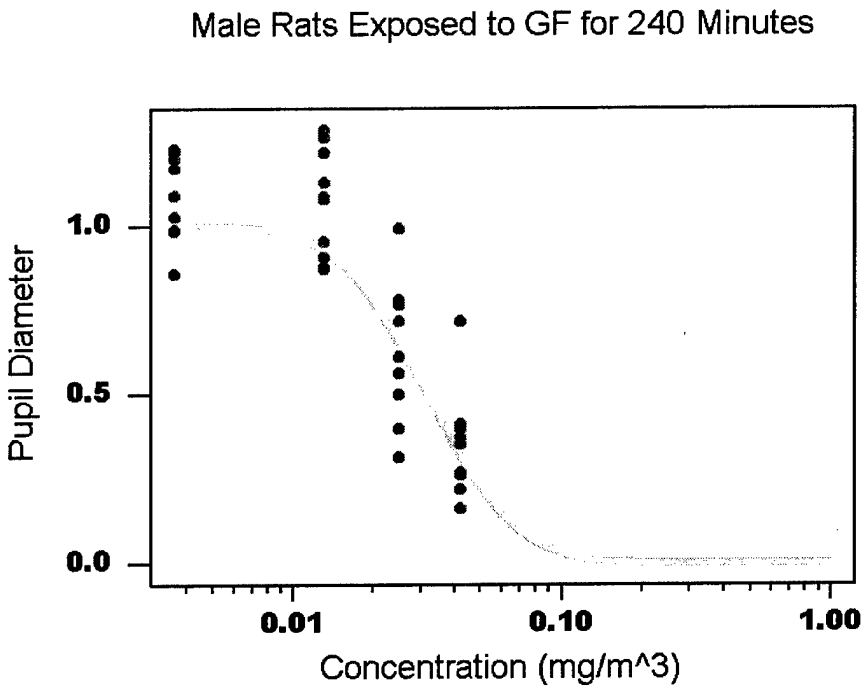

Figure 12. Effects of 240 min GF Vapor Exposure (various fixed concentrations) on Pupil Diameter of Male Rats

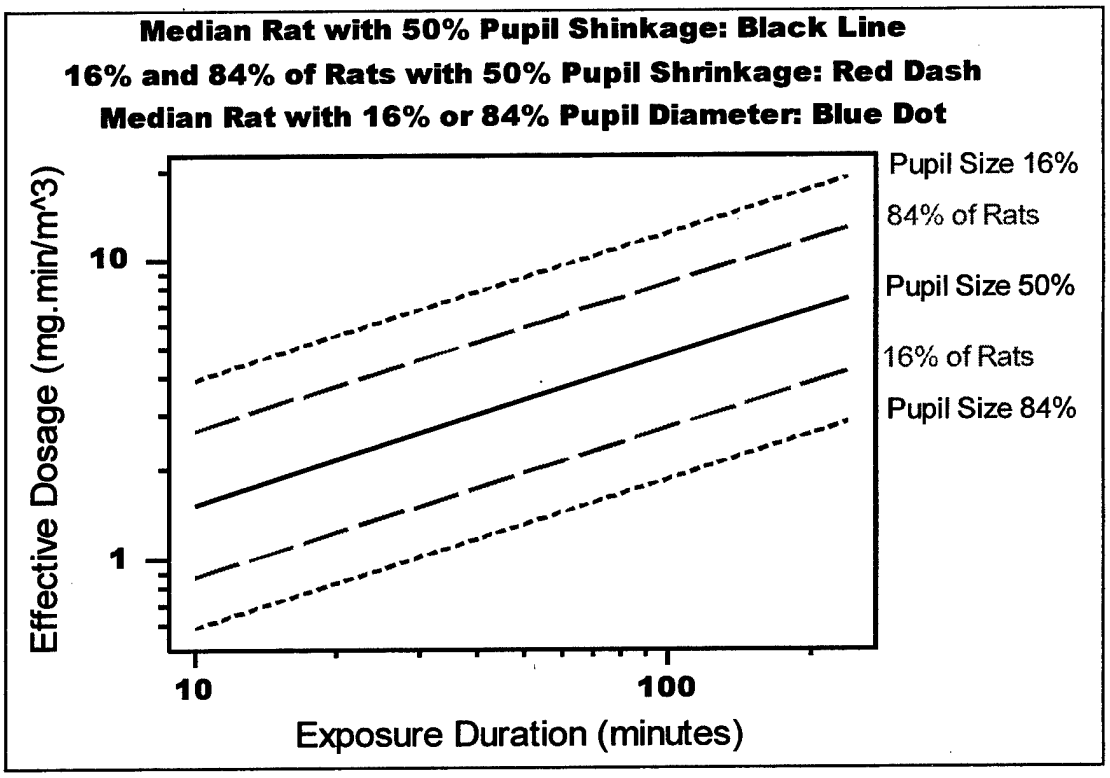

Figure 13. Effect of GF Vapor Exposure on Pupil Size of Male Rats

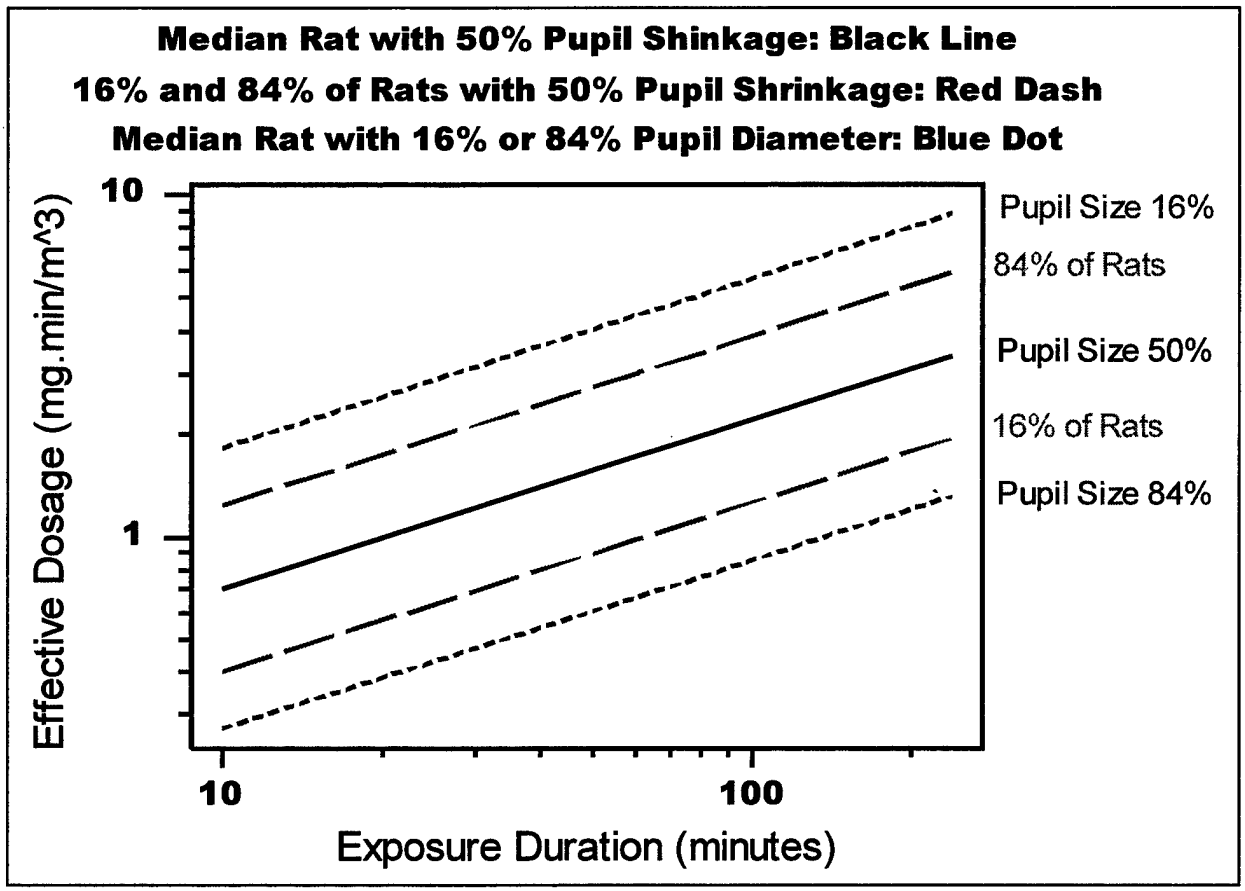

Figure 14. Effect of GF Vapor Exposure on Pupil Size of Female Rats

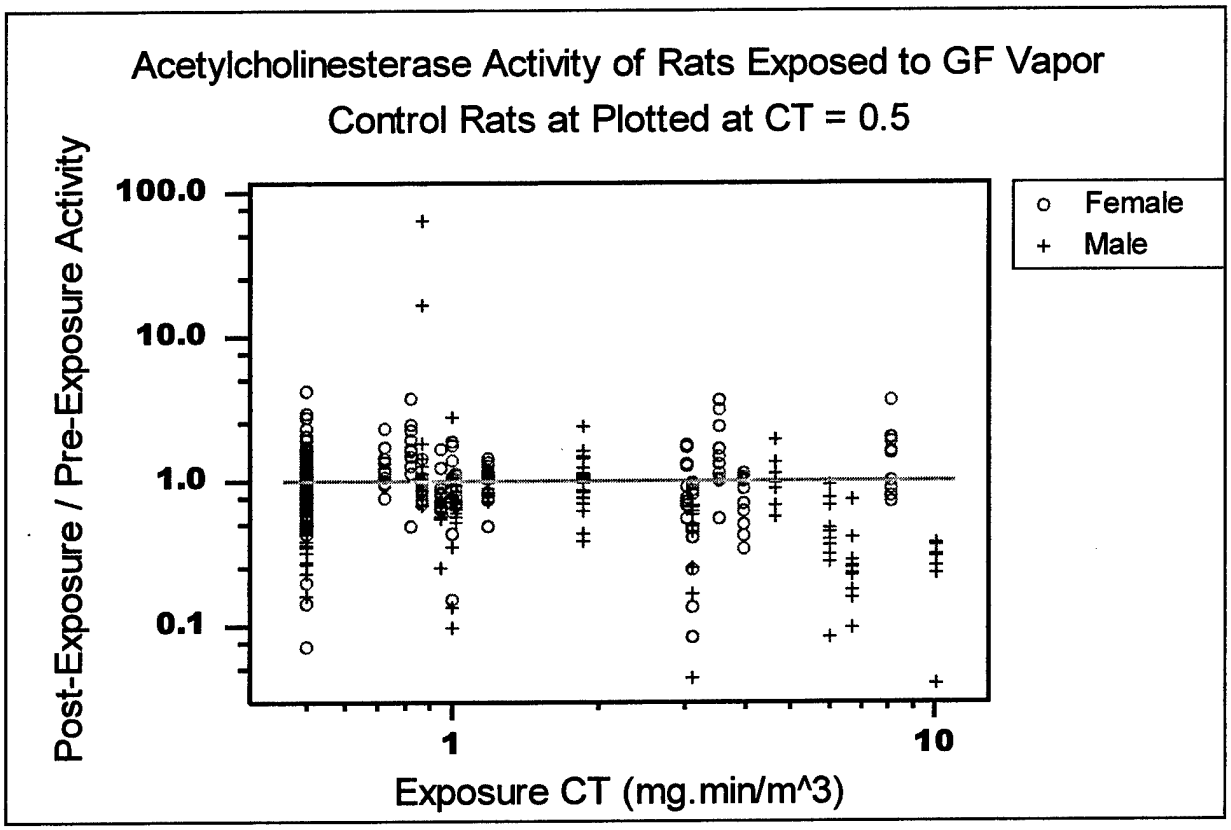

Figure 15. Acetylcholinesterase Activity of Male and Female Rats at 1 Hr After GF Vapor Exposure

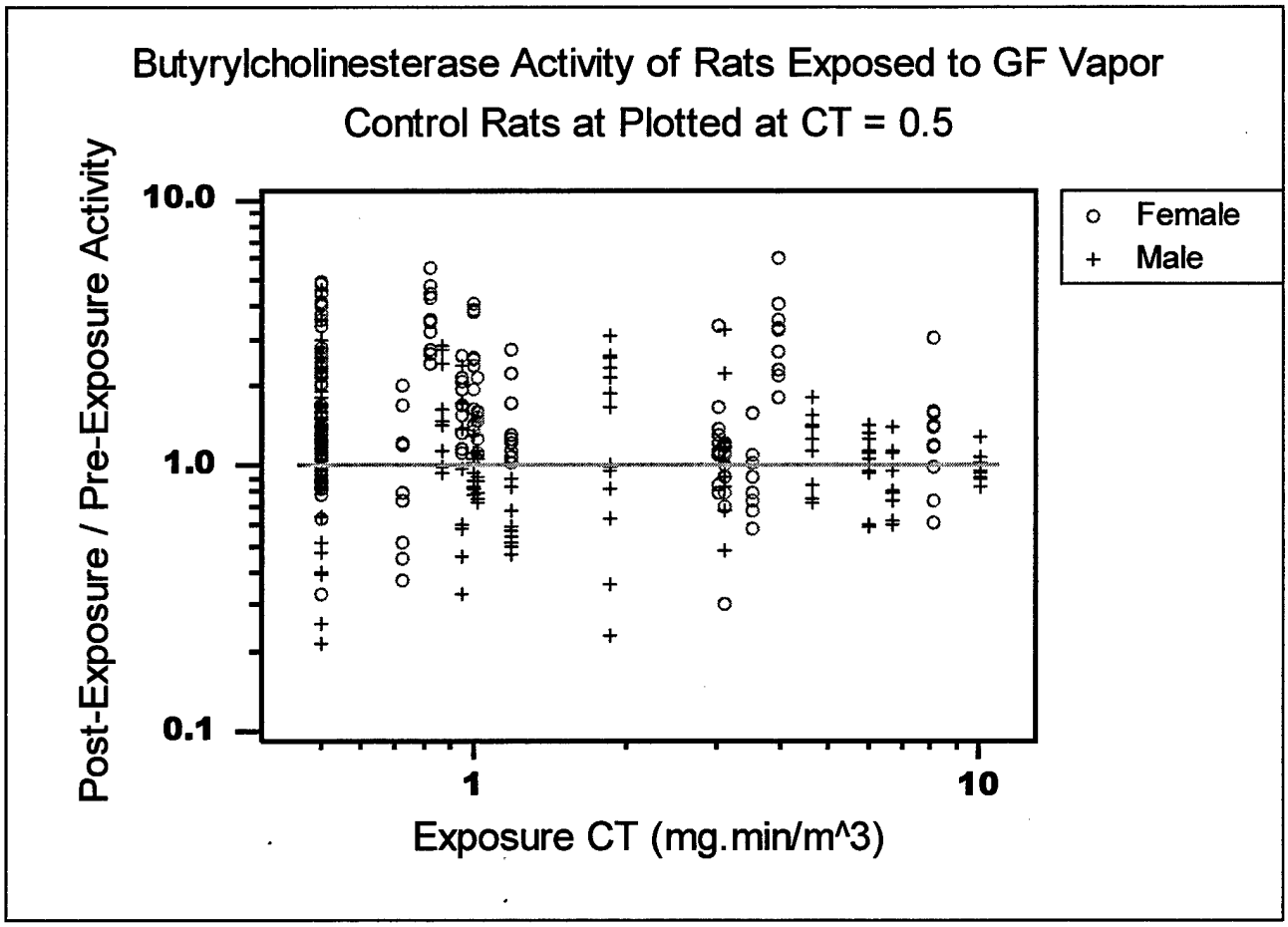

Figure 16. Butyrylcholinesterase Activity of Male and Female Rats at 1 Hr After GF Vapor Exposure

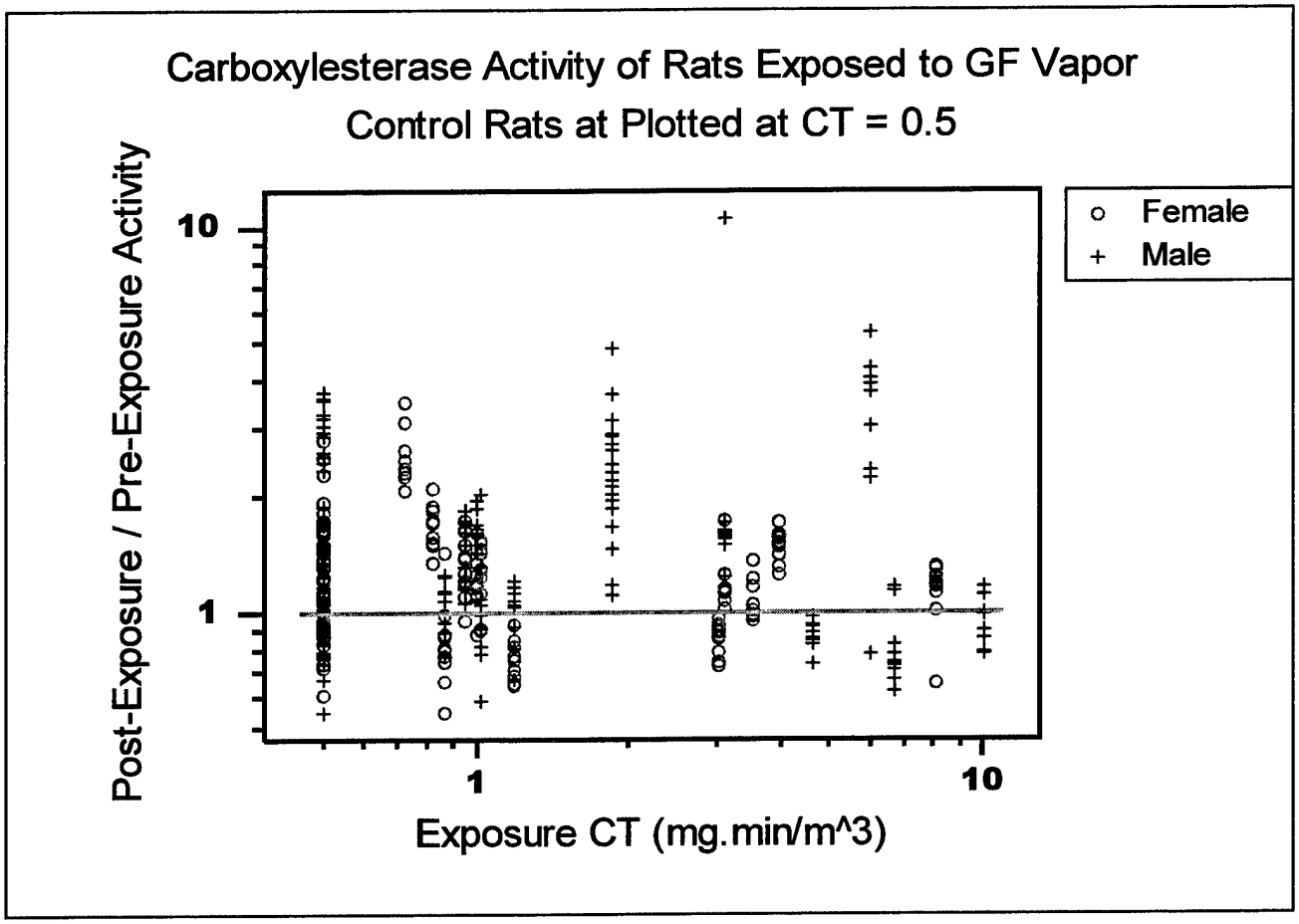

Figure 17. Carboxylesterase Activity of Male and Female Rats at 1 Hr After GF Vapor Exposure

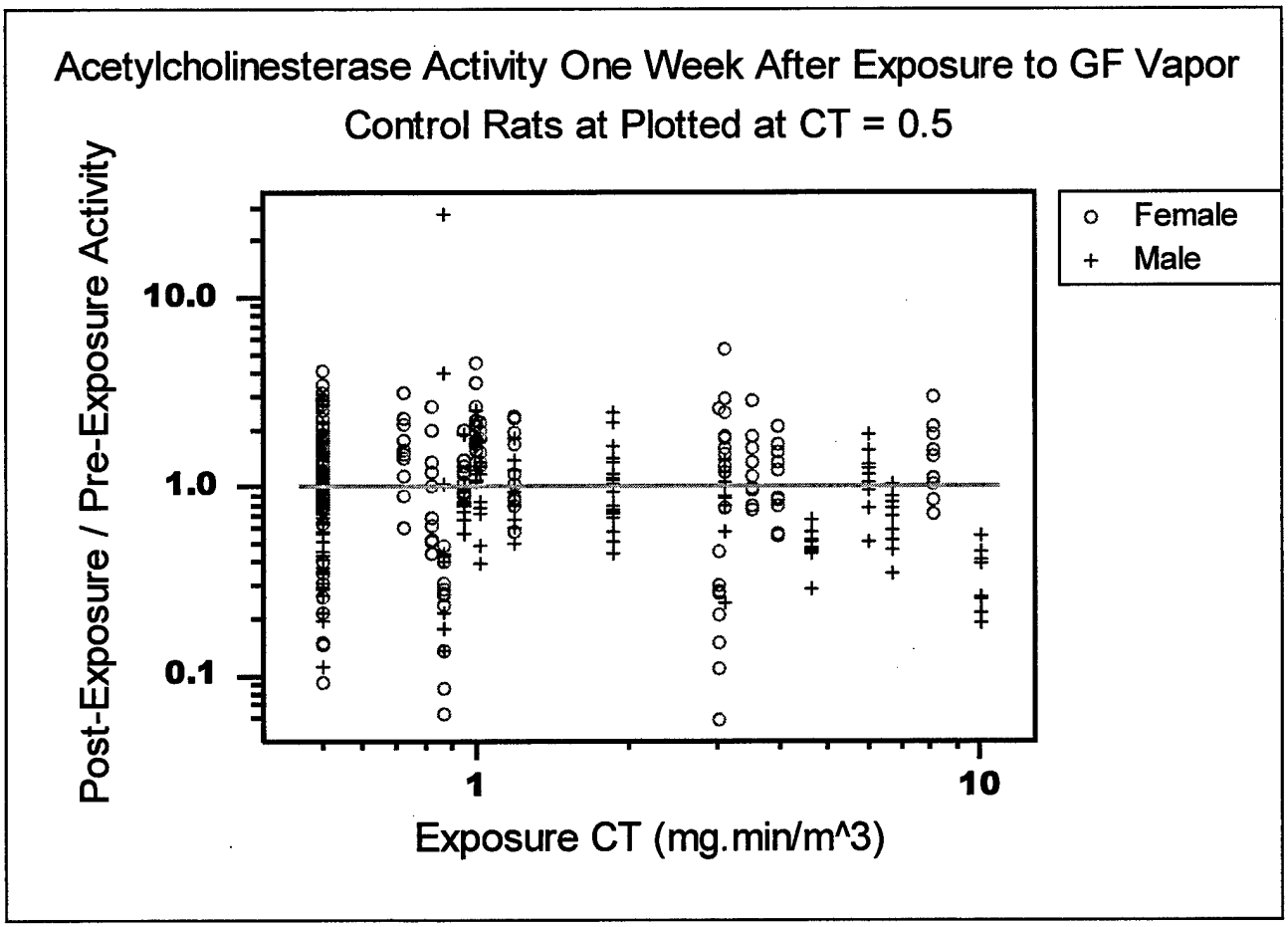

Figure 18. Acetylcholinesterase Activity 1 Week After Exposure to GF Vapor

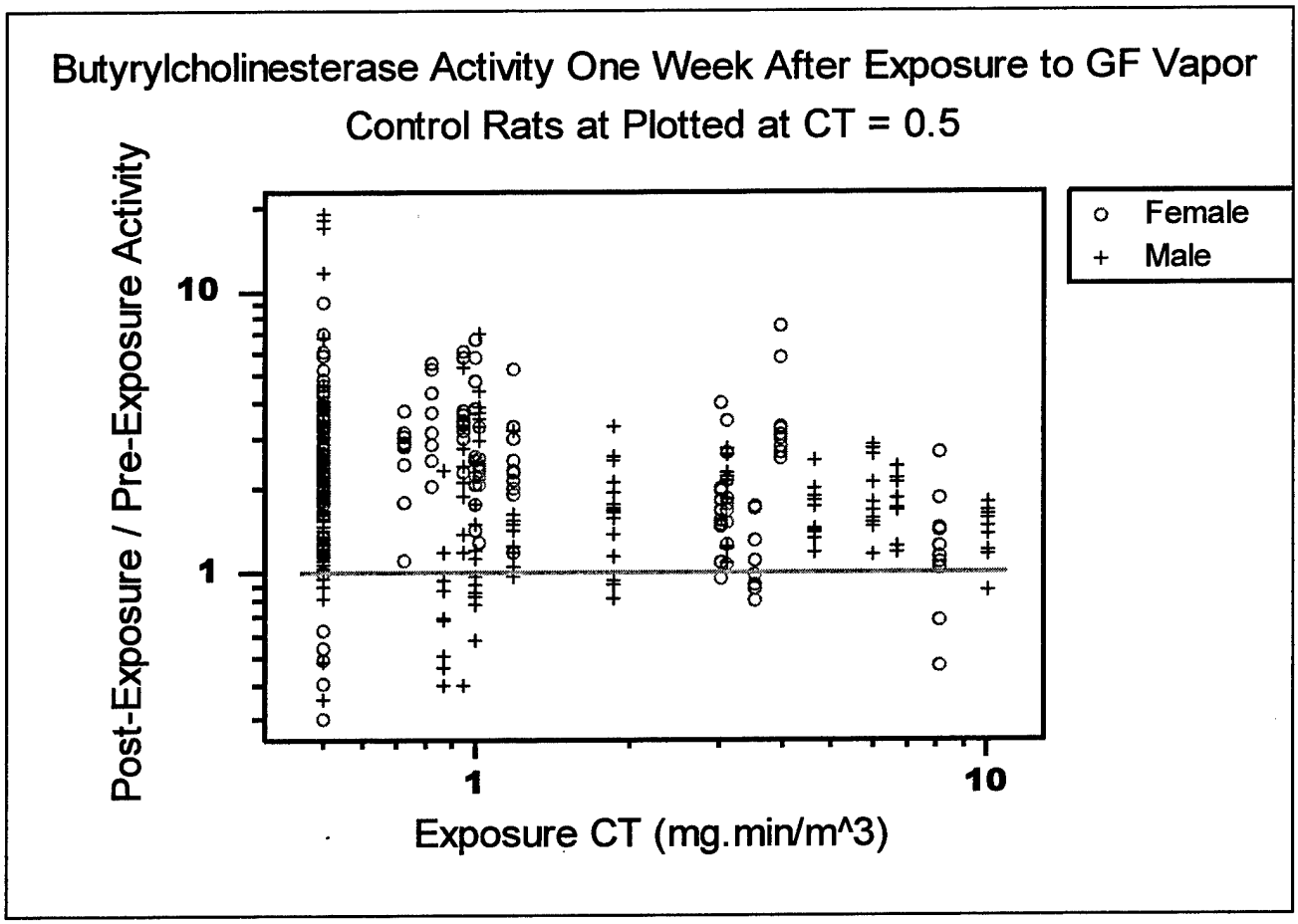

Figure 19. Butyrylcholinesterase Activity 1 Week After Exposure to GF Vapor

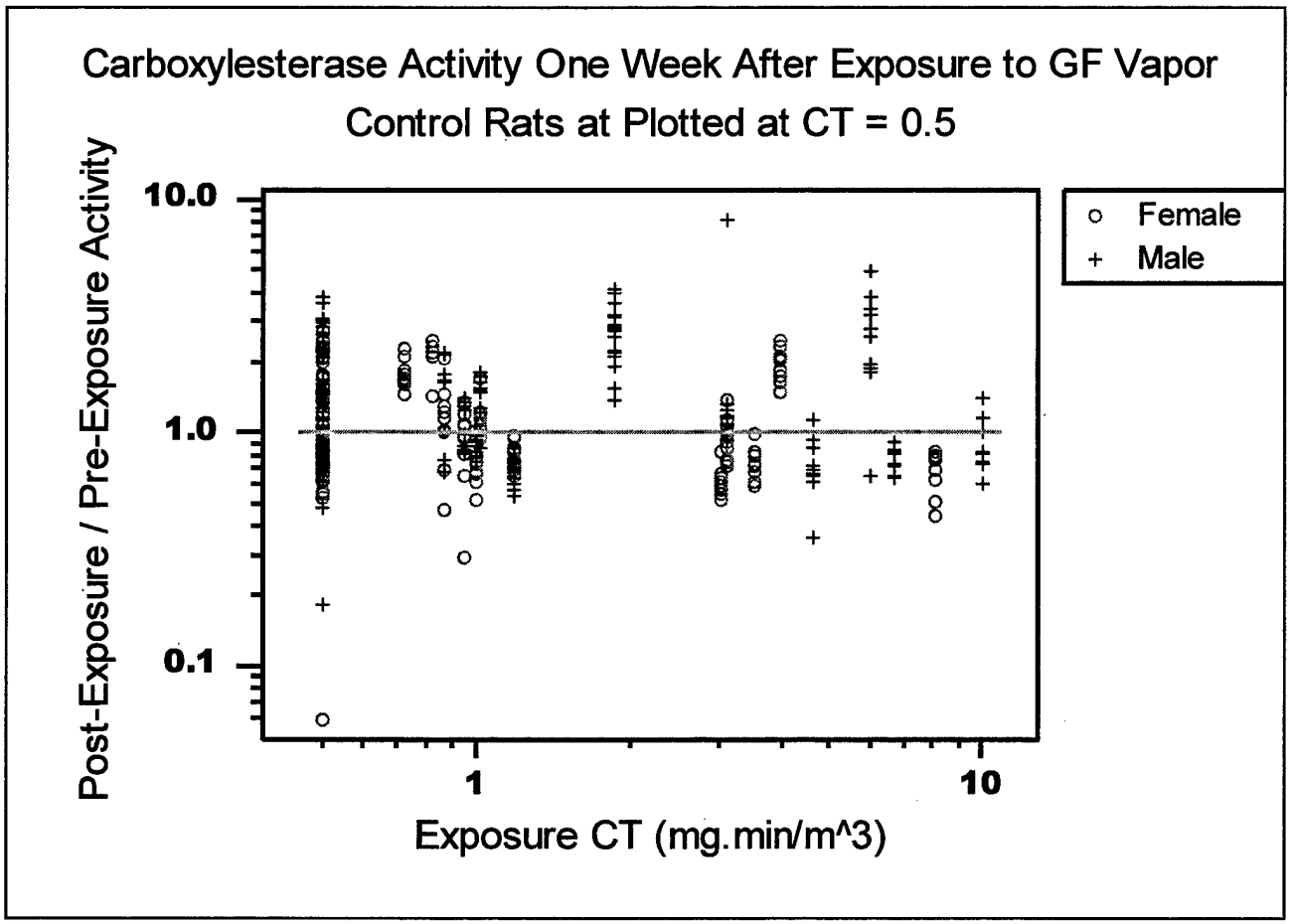

Figure 20. Carboxylesterase Activity 1 Week After Exposure to GF Vapor

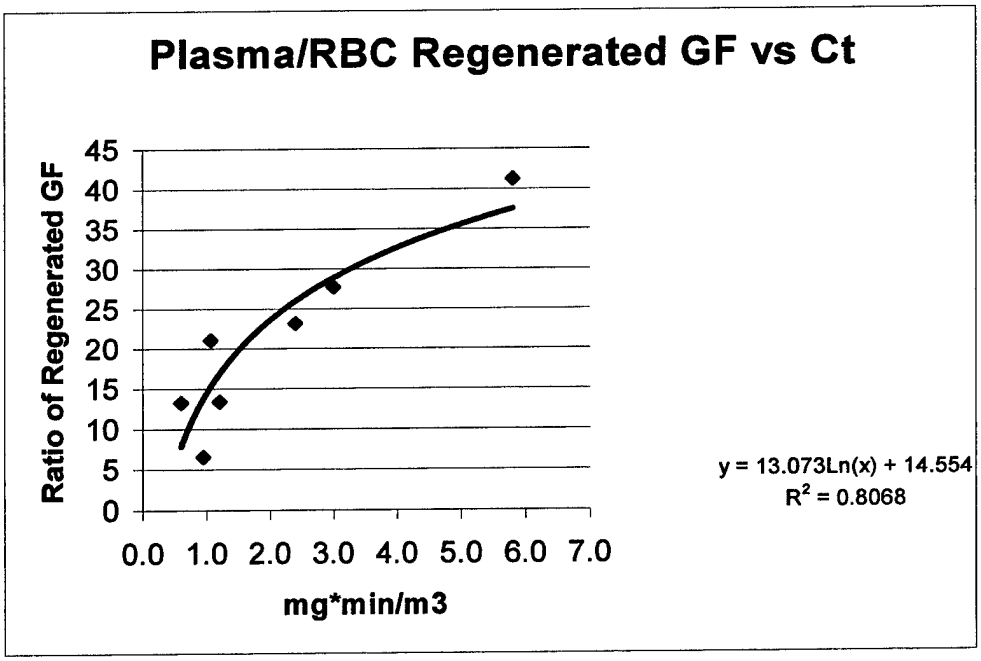

Figure 21. Regenerated GF in Male and Female Rats After Exposure

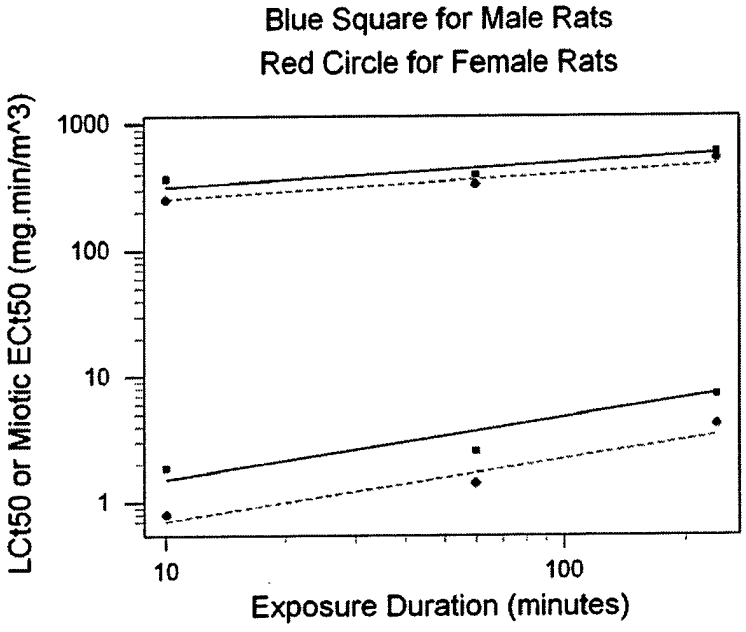

Figure 22. Comparison of GF Miosis (data from Table 2) and Lethality (data from Anthony et al., 2003) in the Rat: Toxic Load Models. Lower lines are miosis; upper lines are lethality.

Table 1. Fraction of Exposed Male and Female Rats that Developed Miosis at each Combination of GF Vapor Concentration (C) and Time (t)

t (min)	C (mg/m^3)	Female	Male
10	0.072	6/10	*
10	0.0947	6/10	1/10
10	0.1183	6/9	2/10
10	0.186	*	4/10
10	0.3586	10/10	*
10	0.465	*	10/10
60	0.0137	3/10	*
60	0.0167	1/10	0/10
60	0.0170	1/10	0/10
60	0.0311	*	3/10
60	0.0508	10/10	*
60	0.112	*	10/10
240	0.0036	0/10	0/10
240	0.013	2/10	0/10
240	0.0166	7/10	*
240	0.0251	*	3/10
240	0.0339	8/10	*
240	0.0422	*	9/10

*Single sex exposed at GF vapor concentration listed.

Table 2. Summary of EC_{50}, ECt_{50}, Slope and Fiducial Intervals for Miosis in Rats Exposed to GF Vapor for 10, 60, or 240 min

Exposure Duration (min)	Slope	STD ERR Slope	EC_{50} (mg/m^3)	95% F.I.	EC_{50} (mg/m^3)	95% F.I.
			Female	Female	Male	Male
10	5.09	0.67	0.080	0.063-0.099	0.184	0.146-0.239
60	5.09	0.67	0.024	0.018-0.031	0.042	0.031-0.059
240	5.09	0.67	0.017	0.014-0.022	0.029	0.023-0.038
Exposure Duration (min)			ECt_{50} (mg-min/m^3)	95% F.I.	ECt_{50} (mg-min/m^3)	95% F.I.
			Female	Female	Male	Male
10			0.796	0.63-0.99	1.843	1.46-2.39
60			1.413	1.13-1.84	2.511	1.86-3.56
240			4.155	3.27-5.25	7.031	5.41-9.19

Table 3. AChE Expressed as U/mL in RBC (Males)

Male Group	Pre-Exposure			1 Hr Post-Exposure			7 Days Post-Exposure		
	Mean	SD	Min, Max	Mean	SD	Min, Max	Mean	SD	Min, Max
6	2.42	0.19	2.19, 2.70	1.36	0.33	0.58, 1.59	2.17	0.84	1.49, 4.27
7	2.34	0.35	1.53, 2.82	1.55	0.14	1.34, 1.76	2.33	0.99	0.60, 3.92
8	1.32	0.83	0.03, 2.54	1.75	0.23	1.17, 1.98	0.62	0.35	0.15, 1.41
9	0.78	0.10	0.58, 0.93	0.62	0.52	0.08, 1.94	1.17	0.31	0.79, 1.66
10	0.92	0.43	0.62, 2.09	0.37	0.17	0.03, 0.60	0.73	0.19	0.50, 1.12
11	0.82	0.11	0.62, 1.00	0.78	0.10	0.57, 0.89	0.83	0.34	0.49, 1.56
12	0.82	0.20	0.51, 1.18	0.81	0.30	0.31, 1.32	0.97	0.33	0.48, 1.45
13	0.73	0.09	0.56, 0.84	0.34	0.18	0.06, 0.63	0.82	0.22	0.41, 1.07
14	0.86	0.20	0.64, 1.20	0.92	0.32	0.46, 1.56	0.67	0.15	0.48, 0.91
15	1.81	0.23	1.49, 2.14	0.50	0.16	0.08, 0.65	0.58	0.23	0.41, 1.14
16	1.64	0.16	1.33, 1.81	1.73	0.59	0.97, 3.17	0.80	0.16	0.50, 1.07
17	1.68	0.17	1.33, 1.89	0.47	0.31	0.18, 1.26	1.17	0.36	0.60, 1.64
Controls	1.40	0.72	0.42, 2.82	0.96	0.59	0.22, 2.41	1.01	0.49	0.27, 2.03

Groups 6-17: n = 10 [Except Group 6 at 1 Hr Post-Exp. (n = 9) and at 7 Days Post-Exp. (n = 9) and Group 8 Pre-Exposure (n = 9)]
Controls: n = 60 (Pre-Exposure); 55 (1 Hr Post-Exp.); 57 (7 Days Post-Exp.)

Table 4. AChE Expressed as U/mL in RBC (Females)

Female Group	Pre-Exposure			1 Hr Post-Exposure			7 Days Post-Exposure		
	Mean	SD	Min, Max	Mean	SD	Min, Max	Mean	SD	Min, Max
6	1.36	0.27	0.74, 1.61	1.17	0.12	1.00, 1.33	1.52	0.21	1.26, 2.00
7	1.48	0.21	1.24, 1.78	1.35	0.15	1.18, 1.65	2.57	0.19	2.30, 2.79
8	1.62	0.37	0.96, 2.13	1.44	0.14	1.21, 1.67	0.42	0.20	0.06, 0.73
9	0.69	0.19	0.35, 0.91	0.66	0.34	0.09, 1.07	1.50	0.38	1.02, 2.23
10	0.56	0.24	0.29, 0.99	0.25	0.14	0.04, 0.48	1.06	0.50	0.38, 1.77
11	0.64	0.12	0.47, 0.87	0.65	0.11	0.38, 0.78	0.87	0.46	0.27, 1.66
12	0.67	0.12	0.53, 0.89	0.84	0.25	0.46, 1.22	1.11	0.59	0.34, 2.56
13	0.75	0.14	0.58, 1.01	0.55	0.16	0.31, 0.77	0.82	0.28	0.39, 1.20
14	0.79	0.28	0.58, 1.54	1.31	0.64	0.70, 2.88	0.85	0.59	0.27, 2.09
15	1.12	0.56	0.44, 1.92	1.41	0.20	1.07, 1.62	1.42	0.30	0.83, 1.80
16	1.17	0.57	0.44, 2.25	1.58	0.29	1.22, 2.07	1.39	0.31	0.83, 1.90
17	1.25	0.50	0.59, 2.09	1.28	0.45	0.75, 1.88	0.41	0.42	0.12, 1.54
Controls	0.97	0.51	0.37, 2.64	1.03	0.57	0.04, 2.77	1.21	0.63	0.11, 2.98

Groups 6, 8-17: n = 10
Group 7: n = 9 (Pre-Exposure); n = 9 (1 Hr Post-Exp.); n = 8 (7 Days Post-Exp.)
Controls: n = 60 (Pre-Exposure); 57 (1 Hr Post-Exp.); 59 (7 Days Post-Exp.)

Table 5. BuChE Expressed as U/mL in Plasma (Males)

Male Group	Pre-Exposure			1 Hr Post-Exposure			7 Days Post-Exposure		
	Mean	SD	Min, Max	Mean	SD	Min, Max	Mean	SD	Min, Max
6	637	431	237, 1634	513	177	260, 811	1178	423	650, 1875
7	404	89	238, 548	365	82	260. 501	1552	204	1116, 1792
8	356	120	192, 561	524	65	439, 640	282	133	109, 442
9	341	58	250, 427	324	63	235, 436	352	104	143, 519
10	309	126	117, 542	343	122	108, 528	514	141	306, 798
11	271	77	161, 432	175	71	99, 297	387	158	186, 758
12	290	114	167, 532	319	135	87, 464	445	135	239, 705
13	259	70	179, 390	264	79	114, 415	503	219	297, 1021
14	322	98	198, 495	736	163	608, 1156	535	125	413, 803
15	338	80	223, 455	329	73	204, 427	473	118	348, 673
16	333	54	232, 390	396	122	269, 640	541	.105	441, 775
17	305	68	186, 381	265	72	162, 367	502	96	343, 640
Controls	396	441	111, 3423	426	179	86, 947	1045	1525	102, 6533

Groups 6-17: n = 10 (n = 9 for Group 6 at 1 Hr Post-Exp. and at 7 Days Post-Exp.; Group 7 Pre-Exposure; Group 8 Pre-Exposure and at 7 Days Post-Exp.; and Group 12 Pre-Exposure and at 1 Hr Post-Exp.)
Controls: n = 60 (Pre-Exposure); 56 (1 Hr Post-Exp.); 58 (7 Days Post-Exp.)

Table 6. BuChE Expressed as U/mL in Plasma (Females)

Female Group	Pre-Exposure			1 Hr Post-Exposure			7 Days Post-Exposure		
	Mean	SD	Min, Max	Mean	SD	Min, Max	Mean	SD	Min, Max
6	1302	397	618, 1908	2085	620	1324, 3249	4598	933	3600, 6596
7	1307	471	839, 2347	1890	454	1287, 2605	2955	1186	1828, 5600
8	NS	NS	NS	2484	864	1330, 4134	1392	882	259, 2997
9	628	443	272, 1571	1343	560	789, 2567	1625	504	978, 2277
10	1088	347	660, 1578	1057	493	250, 1902	2011	750	1105, 3370
11	1598	740	640, 2614	2197	996	842, 4313	3607	1084	1460, 5321
12	883	595	405, 2410	791	448	272, 1748	1968	540	1073, 2682
13	745	383	288, 1631	2111	480	1630, 2933	2528	1132	854, 5012
14	877	397	313, 1513	3008	1096	1522, 5291	2856	1250	1221, 5574
15	1491	630	891, 2850	1824	542	1145, 3011	1700	502	1095, 2618
16	1511	418	743, 1949	1313	414	678, 1986	1565	347	965, 1921
17	1437	409	825, 2144	1856	607	1015, 2825	2394	684	1225, 3314
Controls	1044	537	236, 3252	1843	794	430, 3583	2833	1980	640, 9589

NS = No Samples
Groups 6-17: n = 10 (n = 9 for Group 7 at 1 Hr Post-Exp., for Group 12 and for Group 16 Pre-Exposure; n = 8 for Group 7 Pre-Exposure and at 7 Days Post-Exp.)
Controls: n = 57 (Pre-Exposure); 60 (1 Hr Post-Exp.); 59 (7 Days Post-Exp.)

Table 7. CaE Expressed as μM in Plasma (Males)

Male Group	Pre-Exposure			1 Hr Post-Exposure			7 Days Post-Exposure		
	Mean	SD	Min, Max	Mean	SD	Min, Max	Mean	SD	Min, Max
6	2.93	0.51	2.41, 4.17	4.19	0.44	3.64, 4.75	3.09	0.54	2.24, 4.06
7	2.56	0.53	2.15, 3.99	2.64	1.01	1.67, 5.34	3.56	0.72	2.24, 4.45
8	2.56	0.21	2.33, 3.02	2.66	0.25	2.33, 3.09	3.73	1.38	1.65, 5.27
9	2.49	0.20	2.12, 2.79	4.09	0.34	3.67, 4.84	2.24	0.15	2.05, 2.44
10	2.13	0.65	0.37, 2.68	3.64	0.28	3.30, 3.94	2.69	0.22	2.25, 3.05
11	2.44	0.36	1.91, 3.05	2.35	0.21	1.93, 2.59	1.62	0.10	1.40, 1.75
12	1.31	0.30	1.01, 1.84	3.51	1.01	2.18, 4.90	2.91	0.28	2.54, 3.41
13	1.48	1.03	0.75, 4.30	3.71	0.36	3.17, 4.40	3.12	0.30	2.66, 3.68
14	1.27	0.33	0.86, 1.97	2.37	0.33	1.90, 2.91	3.64	0.57	2.75, 4.72
15	3.27	0.40	2.64, 3.96	3.16	0.45	2.44, 3.94	2.83	0.43	2.40, 3.68
16	3.69	0.31	3.15, 4.26	3.22	0.32	2.61, 3.58	2.70	0.69	1.27, 3.64
17	3.76	0.47	3.00, 4.52	3.00	0.45	2.38, 3.87	2.79	0.29	2.14, 3.09
Controls	2.51	0.97	0.83, 4.27	3.22	0.73	1.17, 4.38	2.92	0.68	0.74, 5.48

Groups 6-17: n = 10 (n = 9 for Group 6 at 1 Hr and 7 Days Post-Exp., Group 8 and Group 12 Pre-Exposure and Group 16 at 7 Days Post-Exp.; n = 8 for Group 8 at 7 Days Post-Exp.)
Controls: n = 60 (Pre-Exposure); 55 (1 Hr Post-Exp.); 58 (7 Days Post-Exp.)

Table 8. CaE Expressed as μM in Plasma (Females)

Female Group	Pre-Exposure			1 Hr Post-Exposure			7 Days Post-Exposure		
	Mean	SD	Min, Max	Mean	SD	Min, Max	Mean	SD	Min, Max
6	2.76	0.41	2.38, 3.71	3.61	0.32	3.13, 4.27	2.63	0.82	0.76, 3.64
7	2.47	0.30	1.88, 2.94	3.15	0.73	1.72, 3.77	2.89	0.25	2.56, 3.22
8	2.82	0.72	1.64, 4.45	2.27	0.21	1.75, 2.44	2.99	0.68	1.84, 4.07
9	2.68	0.31	2.17, 3.21	3.28	0.52	2.70, 4.45	1.84	0.30	1.41, 2.24
10	2.70	0.26	2.14, 3.02	3.20	0.25	2.91, 3.69	2.53	0.34	2.14, 3.16
11	2.71	0.26	2.45, 3.29	2.04	0.20	1.75, 2.39	2.16	0.24	1.75, 2.47
12	1.65	0.20	1.20, 1.86	4.19	0.93	2.83, 6.32	2.94	0.48	1.95, 3.84
13	1.54	0.11	1.38, 1.75	2.30	0.21	1.92, 2.63	3.06	0.41	2.54, 3.71
14	1.46	0.17	1.11, 1.62	2.44	0.41	1.91, 3.34	3.11	0.37	2.28, 3.40
15	3.05	0.42	2.33, 3.72	3.43	0.42	2.43, 3.81	2.05	0.34	1.52, 2.55
16	3.02	0.48	2.34, 3.94	3.22	0.47	2.45, 4.00	2.24	0.35	1.67, 2.66
17	3.39	0.36	2.88, 4.05	2.91	0.41	2.38, 3.79	2.06	0.28	1.72, 2.51
Controls	2.50	0.76	1.32, 4.12	2.96	0.57	2.00, 4.37	2.67	1.02	0.14, 6.82

Groups 6, 8-17: n = 10
Group 7: n = 9 (Pre-Exposure); n = 9 (1 Hr Post-Exp.); n = 8 (7 Days Post-Exp.)
Controls: n = 59 (Pre-Exposure); 59 (1 Hr Post-Exp.); 60 (7 Days Post-Exp.)

LITERATURE CITED

Anthony, J.S., Haley M.V., Manthei, J.H., Way, R.A., Burnett, D.C., Gaviola, B.P., Sommerville, D.R., Crosier, R.B., Mioduszewski, R.J., Thomson, S.A., Crouse, C.L. and Matson, K.L. Inhalation toxicity of GF vapor in rats as a function of exposure and duration and its potency comparison to GB. *ECBC-TR-335.* U.S. Army Edgewood Chemical Biological Center, Aberdeen Proving Ground, MD, 2003.

Barry, B.A. "Errors in Practical Measurement Science, Engineering and Technology." John Wiley & Sons, Inc., NY, 1978.

Bliss, C.I. The method of probits. *Science* 79:38-39, 1934.

Bliss, C.I. The calculation of the dosage-mortality curve. *Annals Appl. Biology* 22:134-167, 1935.

Bliss, C.I. The calculation of the time-mortality curve. *Annals Appl. Biology* 24:815-852, 1937.

Bliss, C.I. "The Statistics of Bioassay with Special References to the Vitamins." Academic Press Inc., New York, 1952.

Cresthull, P., Koon, W.S., McGrath, F.P., and Oberst, F.W. Inhalation effects (incapacitation and mortality) for monkeys exposed to GA, GB, and GF vapors. U.S. Army Chemical Warfare Laboratories Technical Report CWLR 2179, Army Chemical Center, MD, 16 September 1957. (Unclassified/Public Release)

Dunn, M.A., Hackley, B.E., Jr., and Sidell, F. "Pretreatment for Nerve Agent Exposure." In: Textbook of Military Medicine, Part I, Warfare, Weaponry and the Casualty, Medical Aspects of Chemical and Biological Warfare, F.R. Sidell, E.T. Takafuji and D.R. Franz (eds.), Borden Institute, Walter Reed Army Medical Center, Washington, D.C., pp. 181-196, 1997.

Ellman, G.L., Courtney, K.D., Andres, V., Jr., and Featherstone, R.M. A new rapid colormetric determination of acetylcholinesterase activity. *Biochem. Pharm.* 7:88-95, 1961.

Haber, F.R. "Zur Geschichte des Gaskrieges." In: Funf Vortrage aus Jahren 1920-1923, Spinger, Berlin, 1924.

Jakubowski, E.M., Anthony, J.S., Mioduszewski, R.J., Manthei, J.H., Burnett, D.C., Way, R.A., Gaviola, B.I., Montgomery, J.L., Scotto, J.A., Muse, W.T., Whalley, C.E., Matson, K.L., Miller, D.B., Crouse, C.L., Durst, H.D., and Thomson, S.A. Fluoride Ion Regeneration of Cyclosarin (GF) from Rat Blood Following Whole-Body Exposure to Lethal Levels of GF Vapor. Presentation at the 2002 Joint Service Scientific Conference on Chemical and Biological Defense Research, Hunt Valley, Maryland, 19-21 November 2002. (no volume or page number)

Jakubowski, E.M., Mioduszewski, R.J., Hulet, S.W., Manthei, J.H., Benton, B.J., Forster, J.S., Burnett, D.C., Way, R.A., Gaviola, B.I., Edwards, J.L., Muse, W.T., Anthony, J.S., Matson, K.L., Miller, D.B., Crouse, C.L., and Thomson, S.A. Fluoride ion regeneration of sarin (GB) from minipig tissue and fluids after GB inhalation exposure. Presentation at 42nd Annual Meeting of the Society of Toxicology, Salt Lake City, UT, Toxicologist, Vol. 72, No. S-1, page 159, March 2003.

Jakubowski, E.M., Anthony, J.S., Whalley, C.E., Mioduszewski, R.J., Manthei, J.H., Burnett, R.A., Way, R.A., Gaviola, B.I., Edwards, J.L., Scotto, J.A., Muse, W.T., Matson, K.L., Miller, D.B., Crouse, C.L., Durst, H.D., and Thomson, S.A. Fluoride ion regeneration of cyclosarin (GF) from rat blood following whole-body exposure to miosis levels of GF vapor. In preparation, 2004.

Koplovitz, I., Gresham, V.C., Dochterman, L.W., Kaminskis, A., and Stewart, J.R. Evaluation of the toxicity, pathology and treatment of cyclohexylmethylphosphonofluoridate (CMPF) poisoning in rhesus monkeys. *Arch. Toxicol.* 66(9):622-628, 1992.

Koplovitz, I., Schultz, S.M., and Stewart, J.R. Pretreatment and treatment therapy of cyclohexylmethylphosphonofluoridate (GF) poisoning in rodents. *USAMRICD-TR-96-01.* U.S. Army Medical Research Institute of Chemical Defense, Aberdeen Proving Ground, MD, 1 April 1996.

Lennox, W. A method of screening compounds for gross actions in mice. *EASP 100-22.* Edgewood Arsenal, MD, 1969. (Unclassified Report)

MacFarland, H.N. "Designs and Operational Characteristics of Inhalation Exposure Equipment." In: Inhalation Toxicology, Chapter 4, H. Salem (ed.), Marcel Dekker, Inc., New York, 93-120, 1987.

Miller, D.B., Benton, B.J., Hulet, S. W., Mioduszewski, R.J., Whalley, C.E., Carpin, J.C., and Thomson, S.A. An infrared image acquisition and analysis method for quantifying optical responses to chemical agent vapor exposure. 2002 Joint Services Scientific Conference on Chemical & Biological Defense, 19-21 November 2002, Hunt Valley Maryland.

Miller, D.B. Benton, B.J., Hulet, S.W., Mioduszewski, R.J., Whalley, C.E., Carpin, J.C., and Thomson, S.A. An automated infrared image acquisition and analysis method for quantifying optical responses to chemical agent vapor exposure. 29th Annual IEEE Northeast Bioengineering Conference, 22-23 March 2003, New Jersey Institute of Technology, Newark, NJ, 2003a.

Miller, D.B. Benton, B.J., Hulet, S.W., Mioduszewski, R.J., Whalley, C.E., Carpin, J.C., and Thomson, S.A. An image analysis method for quantifying elliptical and partially obstructed pupil areas in response to chemical agent vapor exposure. 29th Annual IEEE Northeast Bioengineering Conference, 22-23 March 2003, New Jersey Institute of Technology, Newark, NJ, 2003b.

MINITAB®, Version 13, Minitab Inc., State College, PA, 2002.

Mioduszewski, R.J., Manthei, J.H., Way, R.A., Burnett, D.C., Gaviola, B.P., Muse, W.T. Jr., Anthony, J.S., Durst, H.D., Sommerville, D.R., Crosier, R.B., Thomson, S.A., and Crouse, C.L. ECBC Low Level Operational Toxicology Program: Phase I - inhalation toxicity of sarin vapor in rats as a function of exposure concentration and duration. *ECBC-TR-183.* U.S. Army Edgewood Chemical Biological Center, Aberdeen Proving Ground, MD, 2001.

Mioduszewski, R.J., Manthei, J.H., Way, R.A., Burnett, D.C., Gaviola, B.P., Muse, W.T. Jr., Thomson, S.A., Sommerville, D.R., Crosier, R.B., Scotto, J.A., McCaskey D.A., Crouse, C.L., and Matson, K.L. Low-Level Sarin Vapor Exposure in Rats: Effect of Exposure Concentration and Duration on Pupil Size. *ECBC-TR-235.* U.S. Army Edgewood Chemical Biological Center, Aberdeen Proving Ground, MD, 2002a.

Mioduszewski, R.J., Manthei, J.H., Way, R.A., Burnett, D.C., Gaviola, B.P., Muse, W.T. Jr., Sommerville, D.R., Crosier, R.B., and Thomson, S.A. Interaction of Exposure Concentration and Duration in Determining Acute Toxic Effects of Sarin Vapor in Rats. *Toxicological Sciences*, 66:176-184, 2002b.

Mioduszewski, R. J., Crosier, R.B., Muse, W.T., Sommerville, D.R., and Thomson, S.A. "Whole-body, low-level sarin vapor exposure in rats: estimating the probability of miosis as a function of exposure concentration and duration." In: Inhalation Toxicology, H. Salem (ed.), Marcel Dekker, NY, submitted March 2003.

Sidell, F.R. "Clinical considerations in nerve agent intoxication." In: Chemical Warfare Agents, S.M. Somani (ed.), New York, NY: Academic Press, 1992.

Sidell, F.R. Nerve Agents. In: Textbook of Military Medicine, Part I, Warfare, Weaponry and the Casualty, Medical Aspects of Chemical and Biological Warfare, F.R. Sidell, E.T. Takafuji and D.R. Franz (eds.), Borden Institute, Walter Reed Army Medical Center, Washington, D.C., pp. 129-179, 1997.

Sommerville, DR, "Relationship Between the Dose-Response Curves for Lethality and Severe Effects for Chemical Warfare Nerve Agents", presented at the Eighth Annual US Army Conference on Applied Statistics. Held 30 October to 1 November 2002, North Carolina State University, Raleigh, NC. Also presented at 2003 Joint Service Scientific Conference on Chemical & Biological Defense Research. Held 17-20 November 2003, Towson, MD.

Whalley, C.E., Benton, B.J., Manthei, J.H., Way, R.A., Jakubowski, E.M., Jr., Burnett, D.C., Gaviola, B.I., Scotto, J.C., Forster, J.S., Crosier, R.B., Sommerville, D.R., Miller, D.B., Crouse, C.L., Matson, K.L., Muse, W., Mioduszewski, R.J., and Thomson, S.A. Low-Level Cyclo-Sarin (GF) Vapor Exposure in Rats: Effect of Exposure Concentration and Duration on Pupil Size. Presentation at the 2002 Joint Service Scientific Conference on Chemical and Biological Defense Research, Hunt Valley, Maryland, 19-21 November 2002. (no volume or page number)

Whalley, C.E., Benton, B.J., Manthei, J.H., Way, R.A., Jakubowski, E.M. Jr., Burnett, D.C., Gaviola, B.I., Scotto, J.C., Forster, J.S., Crosier, R.B., Sommerville, D.R., Miller, D.B., Crouse, C.L., Matson, K.L., Muse, W., Edwards, J.L., Mioduszewski, R.J. and Thomson, S.A. Low-

Level Cyclo-Sarin (GF) Vapor Exposure in Rats: Effect of Exposure Concentration and Duration on Pupil Size. Presentation at the 42nd Annual Meeting of the Society of Toxicology, Salt Lake City, UT, Toxicologist, Vol. 72, No. S-1, page 159, March 2003.

Worek, F., Eyer, P., and Szinicz, L. Inhibition, reactivation and aging kinetics of cyclohexylmethylphosphonofluoridate-inhibited human cholinesterases. *Arch. Toxicol.* 72(9):580-587, 1998.

Young, G.D., and Koplovitz, I. Acute toxicity of cyclohexylmethylphosphonofluoridate (CMPF) in rhesus monkeys: serum biochemical and hematologic changes. *Arch. Toxicol.* 69(6):379-383, 1995.

APPENDIX A

PROBIT ANALYSIS PRINTOUTS FROM MINITAB

The following is a probit analysis (using MINITAB) on the total dataset (both genders and all three exposure durations). The probit analysis was based on a logarithm (base 10) of CT.

Nomenclature

Data Display

Probit Analysis: Miosis, Number versus CT, Group

Female Rats – 10-min exposure duration

Male Rats – 10-min exposure duration

Female Rats – 60-min exposure duration

Male Rats – 60-min exposure duration

Female Rats – 240-min exposure duration

Male Rats – 240-min exposure duration

Potency Comparison between the Six Levels of Group

Summary of ECT_{50} (miosis) by gender

NOMENCLATURE

Gender	M for Male and F for Female
C	GF vapor concentration (mg/m^3)
T	Exposure duration (min)
CT	Concentration-time (mg-min/m^3)
Miosis response	Total number of rats in exposure group having the following binary response 0 for pupil constriction < 50% 1 for pupil constriction equal to or > 50%
Number	Total number of rats in exposure group
Group:	Gender--exposure duration combinations: F10: Female—10-min exposure duration M10: Male—10-min exposure duration F60: Female—60-min exposure duration M60: Male—60-min exposure duration F240: Female—240-min exposure duration M240: Male—240-min exposure duration

Data Display

Row	T	C	CT	Gender	Group	Miosis	Number
1	10	0.0720	0.720	-1	F10	6	10
2	10	0.0947	0.947	-1	F10	6	10
3	10	0.1183	1.183	-1	F10	6	9
4	10	0.3586	3.586	-1	F10	10	10
5	10	0.0947	0.947	1	M10	1	10
6	10	0.1183	1.183	1	M10	2	10
7	10	0.1860	1.860	1	M10	4	10
8	10	0.4650	4.650	1	M10	10	10
9	60	0.0137	0.822	-1	F60	3	10
10	60	0.0167	1.002	-1	F60	1	10
11	60	0.0170	1.020	-1	F60	1	10
12	60	0.0508	3.048	-1	F60	10	10
13	60	0.0167	1.002	1	M60	0	10
14	60	0.0170	1.020	1	M60	0	10
15	60	0.0311	1.866	1	M60	3	10
16	60	0.1120	6.720	1	M60	10	10
17	240	0.0036	0.864	-1	F240	0	10
18	240	0.0130	3.120	-1	F240	2	10
19	240	0.0166	3.984	-1	F240	7	10
20	240	0.0339	8.136	-1	F240	8	10
21	240	0.0036	0.864	1	M240	0	10
22	240	0.0130	3.120	1	M240	0	10
23	240	0.0251	6.024	1	M240	3	10
24	240	0.0422	10.128	1	M240	9	10

Probit Analysis: Miosis, Number versus CT, Group

Distribution: Lognormal base 10

Response Information

Variable	Value	Count
Miosis	Success	102
	Failure	137
Number	Total	239

Factor Information

Factor	Levels	Values
Group	6	F10 M10 F60 M60 F240 M240

Estimation Method: Maximum Likelihood

Regression Table

Variable	Coef	Standard Error	Z	P
Constant	0.5008	0.2410	2.08	0.038
CT	5.0559	0.6685	7.56	0.000
Group				
M10	-1.8434	0.3810	-4.84	0.000
F60	-1.2606	0.3492	-3.61	0.000
M60	-2.5221	0.4596	-5.49	0.000
F240	-3.6279	0.5700	-6.37	0.000
M240	-4.7831	0.6897	-6.94	0.000
Natural Response	0.000			

Test for equal slopes: Chi-Square = 5.4297, DF = 5, P-Value = 0.366
Log-Likelihood = -86.741

Multiple degree of freedom test

Term	Chi-Square	DF	P
Group	53.481	5	0.000

Goodness-of-Fit Tests

Method	Chi-Square	DF	P
Pearson	16.365	17	0.498
Deviance	16.744	17	0.472

Female Rats—10-min exposure duration

Group = F10

Tolerance Distribution

Parameter Estimates

Parameter	Estimate	Standard Error	95.0% Normal CI Lower	Upper
Location	-0.09906	0.04805	-0.19324	-0.00487
Scale	0.19779	0.02615	0.15264	0.25630

Table of Percentiles

Percent	Percentile	Standard Error	95.0% Fiducial CI Lower	Upper
1	0.2759	0.05306	0.1697	0.3775
2	0.3124	0.05593	0.1995	0.4193
3	0.3380	0.05776	0.2208	0.4484
4	0.3587	0.05916	0.2383	0.4717
5	0.3764	0.06030	0.2535	0.4918
6	0.3921	0.06128	0.2671	0.5096
7	0.4065	0.06216	0.2796	0.5258
8	0.4198	0.06296	0.2913	0.5409
9	0.4323	0.06369	0.3023	0.5550
10	0.4441	0.06438	0.3127	0.5684
20	0.5426	0.07004	0.4011	0.6809
30	0.6269	0.07521	0.4776	0.7795
40	0.7093	0.08097	0.5521	0.8787
50	**0.7961**	**0.08808**	**0.6295**	**0.9868**
60	0.8934	0.09754	0.7147	1.1132
70	1.0108	0.1111	0.8145	1.2728
80	1.1679	0.1330	0.9429	1.4986
90	1.4270	0.1770	1.1433	1.8990
91	1.4660	0.1843	1.1725	1.9620
92	1.5096	0.1928	1.2047	2.0332
93	1.5590	0.2026	1.2410	2.1149
94	1.6161	0.2143	1.2825	2.2106
95	1.6838	0.2286	1.3311	2.3257
96	1.7669	0.2468	1.3900	2.4696
97	1.8748	0.2712	1.4653	2.6600
98	2.0284	0.3078	1.5706	2.9383
99	2.2965	0.3756	1.7494	3.4425

Male Rats—10-min exposure duration

Group = M10

Tolerance Distribution

Parameter Estimates

Parameter	Estimate	Standard Error	95.0% Normal CI Lower	Upper
Location	0.26555	0.05222	0.16319	0.36790
Scale	0.19779	0.02615	0.15264	0.25630

Table of Percentiles

Percent	Percentile	Standard Error	95.0% Fiducial CI Lower	Upper
1	0.6389	0.1045	0.4284	0.8416
2	0.7233	0.1104	0.5010	0.9391
3	0.7826	0.1144	0.5527	1.0078
4	0.8304	0.1176	0.5948	1.0635
5	0.8714	0.1204	0.6310	1.1116
6	0.9079	0.1229	0.6633	1.1546
7	0.9411	0.1252	0.6928	1.1941
8	0.9719	0.1274	0.7202	1.2308
9	1.0008	0.1295	0.7459	1.2655
10	1.0282	0.1316	0.7702	1.2985
20	1.2563	0.1506	0.9716	1.5817
30	1.4515	0.1705	1.1402	1.8370
40	1.6422	0.1936	1.3005	2.0986
50	**1.8431**	**0.2216**	**1.4641**	**2.3872**
60	2.0685	0.2575	1.6418	2.7264
70	2.3403	0.3061	1.8486	3.1551
80	2.7040	0.3793	2.1146	3.7597
90	3.3039	0.5167	2.5322	4.8243
91	3.3942	0.5389	2.5932	4.9911
92	3.4951	0.5641	2.6609	5.1795
93	3.6095	0.5932	2.7370	5.3954
94	3.7417	0.6275	2.8243	5.6479
95	3.8984	0.6691	2.9266	5.9514
96	4.0909	0.7213	3.0511	6.3302
97	4.3406	0.7911	3.2104	6.8311
98	4.6964	0.8939	3.4336	7.5621
99	5.3171	1.0821	3.8140	8.8840

Female Rats—60-min exposure duration

Group = F60

Tolerance Distribution

Parameter Estimates

Parameter	Estimate	Standard Error	95.0% Normal CI Lower	Upper
Location	0.15027	0.05176	0.04883	0.25172
Scale	0.19779	0.02615	0.15264	0.25630

Table of Percentiles

Percent	Percentile	Standard Error	95.0% Fiducial CI Lower	Upper
1	0.4899	0.07554	0.3368	0.6362
2	0.5547	0.07965	0.3936	0.7105
3	0.6002	0.08251	0.4340	0.7630
4	0.6368	0.08484	0.4667	0.8056
5	0.6682	0.08688	0.4948	0.8425
6	0.6962	0.08875	0.5199	0.8755
7	0.7217	0.09050	0.5428	0.9059
8	0.7454	0.09216	0.5640	0.9342
9	0.7675	0.09377	0.5838	0.9609
10	0.7885	0.09534	0.6026	0.9864
20	0.9634	0.1104	0.7573	1.2061
30	1.1131	0.1266	0.8858	1.4054
40	1.2594	0.1455	1.0072	1.6105
50	**1.4134**	**0.1685**	**1.1308**	**1.8371**
60	1.5863	0.1977	1.2647	2.1037
70	1.7947	0.2372	1.4203	2.4407
80	2.0737	0.2962	1.6205	2.9159
90	2.5337	0.4062	1.9351	3.7521
91	2.6029	0.4239	1.9811	3.8831
92	2.6803	0.4440	2.0321	4.0309
93	2.7680	0.4671	2.0895	4.2005
94	2.8694	0.4944	2.1553	4.3987
95	2.9896	0.5274	2.2325	4.6370
96	3.1372	0.5689	2.3264	4.9343
97	3.3287	0.6242	2.4466	5.3274
98	3.6015	0.7055	2.6152	5.9011
99	4.0776	0.8542	2.9025	6.9384

Male Rats—60-min exposure duration

Group = M60

Tolerance Distribution

Parameter Estimates

Parameter	Estimate	Standard Error	95.0% Normal CI Lower	Upper
Location	0.39979	0.06965	0.26328	0.53630
Scale	0.19779	0.02615	0.15264	0.25630

Table of Percentiles

Percent	Percentile	Standard Error	95.0% Fiducial CI Lower	Upper
1	0.8703	0.1583	0.5687	1.1990
2	0.9853	0.1712	0.6612	1.3459
3	1.0661	0.1804	0.7265	1.4501
4	1.1311	0.1880	0.7793	1.5350
5	1.1870	0.1946	0.8247	1.6085
6	1.2367	0.2006	0.8650	1.6745
7	1.2820	0.2061	0.9018	1.7350
8	1.3240	0.2114	0.9358	1.7915
9	1.3633	0.2163	0.9676	1.8449
10	1.4006	0.2211	0.9977	1.8957
20	1.7113	0.2643	1.2460	2.3324
30	1.9773	0.3060	1.4537	2.7250
40	2.2371	0.3510	1.6518	3.1250
50	**2.5106**	**0.4026**	**1.8552**	**3.5631**
60	2.8177	0.4654	2.0777	4.0745
70	3.1879	0.5473	2.3386	4.7169
80	3.6834	0.6662	2.6767	5.6173
90	4.5005	0.8821	3.2119	7.1933
91	4.6235	0.9165	3.2903	7.4396
92	4.7610	0.9554	3.3775	7.7174
93	4.9168	1.0002	3.4756	8.0357
94	5.0969	1.0528	3.5881	8.4078
95	5.3103	1.1162	3.7203	8.8547
96	5.5726	1.1957	3.8810	9.4120
97	5.9127	1.3014	4.0871	10.1482
98	6.3973	1.4563	4.3761	11.2216
99	7.2430	1.7380	4.8693	13.1604

Female Rats—240-min exposure duration

Group = F240

Tolerance Distribution

Parameter Estimates

Parameter	Estimate	Standard Error	95.0% Normal CI Lower	Upper
Location	0.61852	0.05048	0.51957	0.71746
Scale	0.19779	0.02615	0.15264	0.25630

Table of Percentiles

Percent	Percentile	Standard Error	95.0% Fiducial CI Lower	Upper
1	1.4401	0.2673	0.9058	1.9556
2	1.6304	0.2822	1.0627	2.1752
3	1.7641	0.2920	1.1752	2.3289
4	1.8717	0.2996	1.2670	2.4527
5	1.9642	0.3059	1.3466	2.5590
6	2.0464	0.3114	1.4179	2.6537
7	2.1214	0.3164	1.4832	2.7402
8	2.1908	0.3210	1.5440	2.8205
9	2.2559	0.3253	1.6013	2.8959
10	2.3176	0.3293	1.6556	2.9676
20	2.8317	0.3644	2.1125	3.5736
30	3.2719	0.3981	2.5040	4.1096
40	3.7017	0.4362	2.8822	4.6522
50	**4.1545**	**0.4829**	**3.2731**	**5.2464**
60	4.6626	0.5438	3.7009	5.9421
70	5.2752	0.6289	4.2008	6.8211
80	6.0951	0.7614	4.8442	8.0628
90	7.4472	1.0196	5.8515	10.2565
91	7.6508	1.0621	5.9982	10.6010
92	7.8782	1.1107	6.1609	10.9901
93	8.1360	1.1670	6.3437	11.4364
94	8.4340	1.2338	6.5530	11.9588
95	8.7872	1.3149	6.7984	12.5869
96	9.2211	1.4177	7.0963	13.3713
97	9.7841	1.5555	7.4773	14.4090
98	10.5859	1.7601	8.0103	15.9247
99	11.9852	2.1380	8.9171	18.6680

Male Rats—240-min exposure duration

Group = M240

Tolerance Distribution

Parameter Estimates

Parameter	Estimate	Standard Error	95.0% Normal CI Lower	Upper
Location	0.84699	0.05664	0.73597	0.95800
Scale	0.19779	0.02615	0.15264	0.25630

Table of Percentiles

Percent	Percentile	Standard Error	95.0% Fiducial CI Lower	Upper
1	2.4370	0.4563	1.5382	3.3351
2	2.7591	0.4851	1.8006	3.7180
3	2.9853	0.5045	1.9880	3.9869
4	3.1675	0.5199	2.1407	4.2042
5	3.3239	0.5329	2.2727	4.3912
6	3.4631	0.5445	2.3907	4.5581
7	3.5900	0.5551	2.4987	4.7108
8	3.7075	0.5649	2.5990	4.8527
9	3.8177	0.5742	2.6934	4.9862
10	3.9220	0.5830	2.7828	5.1131
20	4.7921	0.6607	3.5309	6.1921
30	5.5369	0.7356	4.1675	7.1512
40	6.2644	0.8185	4.7800	8.1239
50	**7.0305**	**0.9169**	**5.4121**	**9.1888**
60	7.8904	1.0412	6.1042	10.4335
70	8.9271	1.2096	6.9145	12.0017
80	10.3146	1.4640	7.9610	14.2088
90	12.6028	1.9455	9.6071	18.0920
91	12.9472	2.0238	9.8476	18.7005
92	13.3321	2.1129	10.1144	19.3874
93	13.7684	2.2159	10.4144	20.1750
94	14.2727	2.3376	10.7581	21.0963
95	14.8704	2.4852	11.1614	22.2035
96	15.6047	2.6713	11.6513	23.5854
97	16.5573	2.9202	12.2784	25.4127
98	17.9143	3.2881	13.1566	28.0797
99	20.2823	3.9643	14.6521	32.9030

Potency Comparison between the Six Levels of Group

Table of Relative Potency

Factor: Group

Comparison	Relative Potency	95.0% Fiducial CI Lower	Upper
F10 VS M10	2.3153	1.6911	3.3270
F10 VS F60	1.7755	1.3024	2.5676
F10 VS M60	3.1539	2.1757	4.8909
F10 VS F240	5.2188	3.8000	7.2741
F10 VS M240	8.8317	6.3143	12.6780
M10 VS F60	0.7669	0.5531	1.0747
M10 VS M60	1.3622	0.9263	2.0416
M10 VS F240	2.2541	1.5756	3.1181
M10 VS M240	3.8145	2.6357	5.3983
F60 VS M60	1.7763	1.2087	2.6327
F60 VS F240	2.9393	2.0451	4.0417
F60 VS M240	4.9741	3.4253	6.9890
M60 VS F240	1.6547	1.0751	2.4162
M60 VS M240	2.8003	1.8065	4.1643
F240 VS M240	1.6923	1.1934	2.4268

Note: If the 95% fiducial CI do not overlap the value of 1.0, then there is a statistically significant difference between the two group levels being compared.

Summary of ECT_{50} (miosis) by gender

Row	Time	ECT50 Female	ECT50 Male
1	10	0.796	1.843
2	60	1.413	2.511
3	240	4.155	7.031

APPENDIX B

SYNONYMS FOR GF

GF (CAS number 329-99-7)

Synonyms:

BRN 2327087
CF Me Ester
CMPF
Cyclohexyl Methylphosphonofluoridate
Cyclohexyl Sarin
Cyclosarin
Cyclosin
EA 1212
Methyl Cyclohexylfluorophosphonate
O-Cyclohexyl methylphosphonofluoridate
Phosphonofluoridic Acid, Methyl-, Cyclohexyl Ester
T.2139

Other Registry Numbers:

38184-40-6
74192-15-7

RTECS number: TA8225000

Molecular Formula: C7 H14 F O2 P

Blank

APPENDIX C

T_{99} TABLE FOR GF EXPOSURES

Group	Sex	T_{99} (min)
6	MF	6.4
7	MF	6.8
8	MF	5.7
9	MF	6.4
10	MF	5.7
11	MF	6.7
12	MF	6.4
13	M	6.1
13	F	6.6
14	MF	6.5
15	M	6.0
15	F	6.5
16	M	6.0
16	F	6.5
17	MF	6.5

Blank

APPENDIX D

ESTERASE RAW DATA

Legend

#c = Control Group
ns = No Specimen
HCT = Hematocrit (%)
AChE & BuChE expressed in U/mL
CaE expressed in μM
° = Hr
DEAD = animal died of causes unrelated to exposure

6	**M**	**0.0947 mg/m3**	**10 min**
6	**F**	**0.0947 mg/m3**	**10 min**
7	**M**	**0.0170 mg/m3**	**60 min**
7	**F**	**0.0170 mg/m3**	**60 min**
8	**M**	**0.0036 mg/m3**	**240 min**
8	**F**	**0.0036 mg/m3**	**240 min**
9	**M**	**0.0167 mg/m3**	**60 min**
9	**F**	**0.0167 mg/m3**	**60 min**
10	**M**	**0.013 mg/m3**	**240 min**
10	**F**	**0.013 mg/m3**	**240 min**
11	**M**	**0.1183 mg/m3**	**10 min**
11	**F**	**0.1183 mg/m3**	**10 min**
12	**M**	**0.186 mg/m3**	**10 min**
12	**F**	**0.072 mg/m3**	**10 min**
13	**M**	**0.0251 mg/m3**	**240 min**
13	**F**	**0.0166 mg/m3**	**240 min**
14	**M**	**0.0311 mg/m3**	**60 min**
14	**F**	**0.0137 mg/m3**	**60 min**
15	**M**	**0.0422 mg/m3**	**240 min**
15	**F**	**0.0339 mg/m3**	**240 min**
16	**M**	**0.465 mg/m3**	**10 min**
16	**F**	**0.355 mg/m3**	**10 min**
17	**M**	**0.112 mg/m3**	**60 min**
17	**F**	**0.0508 mg/m3**	**10 min**

GROUP	SEX	ID #	Pre HCT	Pre AChE	Pre BuChE	Pre CaE	1° HCT	1° Post AChE	1° Post BuChE	1° Post CaE	7 Day HCT	7 Day AChE	7 Day BuChE	7 Day CaE
6	M	43	45	2.60	237	2.74	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD
6	M	52	40	2.47	408	4.17	38	1.53	705	4.42	36	1.95	965	3.54
6	M	57	41	2.70	342	2.48	41	1.53	811	4.01	45	1.82	717	3.35
6	M	62	41	2.30	594	2.88	36	0.58	582	3.81	43	1.71	817	4.06
6	M	66	40	2.57	446	2.41	43	1.44	260	4.11	42	2.53	1218	3.10
6	M	68	43	2.27	490	2.74	41	1.22	293	4.75	ns	4.27	1611	2.24
6	M	70	41	2.63	772	2.55	38	ns	446	4.69	37	1.49	1444	3.21
6	M	71	41	2.25	349	3.06	41	1.59	477	3.69	ns	2.10	1875	2.69
6	M	76	43	2.19	1634	3.14	39	1.44	538	3.64	41	1.79	650	2.58
6	M	79	41	2.24	1099	3.09	40	1.51	501	4.63	43	1.86	1305	3.02
6c	M	41	45	1.08	297	2.44	41	1.77	391	3.62	40	1.05	897	2.26
6c	M	74	44	2.63	337	2.58	40	ns	947	4.37	40	1.72	1313	2.58
6c	M	80	43	2.27	1626	3.27	39	ns	767	4.38	25	1.97	1907	2.58
6c	M	87	40	2.07	3423	4.09	38	1.28	730	3.68	43	1.81	1644	0.74
6c	M	64	41	2.30	370	2.30	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD
6	F	105	45	1.57	1908	2.75	37	1.13	3249	3.32	31	2.00	6596	2.65
6	F	107	47	1.61	1470	2.63	39	1.01	2840	3.68	37	1.71	5015	0.76
6	F	109	45	1.23	1344	2.63	40	1.00	2091	3.63	31	1.43	5031	2.13
6	F	114	43	1.53	618	3.00	37	1.33	1597	3.56	37	1.43	3779	3.18
6	F	119	39	1.06	1142	3.71	39	1.29	1324	3.53	35	1.47	3619	2.41
6	F	123	47	0.74	1209	2.47	39	1.24	2513	3.71	ns	1.47	4058	3.29
6	F	128	49	1.38	1893	2.46	39	1.24	2135	3.13	40	1.64	4255	3.32
6	F	132	44	1.49	899	3.06	39	1.24	1943	3.37	44	1.40	5248	3.64
6	F	133	47	1.40	1208	2.46	40	1.23	1609	4.27	ns	1.26	3600	2.35
6	F	141	46	1.54	1327	2.38	37	1.01	1547	3.89	ns	1.40	4777	2.59
6c	F	98	45	1.02	1553	2.06	38	1.19	1881	2.73	ns	1.91	3853	1.93
6c	F	116	42	0.99	498	2.63	41	1.42	2048	Ns	36	1.59	4599	3.24
6c	F	110	44	0.97	1908	2.61	40	ns	1831	3.57	34	1.59	4547	2.52
6c	F	117	44	1.74	896	2.39	40	1.11	1040	3.86	26	2.00	3000	0.14
6c	F	137	47	1.53	735	2.67	41	ns	1757	3.71	33	1.26	3241	3.22
7	M	48	42	2.66	406	2.66	41	1.61	297	2.42	42	1.90	1792	4.12
7	M	53	42	2.29	365	2.29	41	1.70	266	2.10	41	1.89	1409	3.42
7	M	55	42	2.41	342	2.41	41	1.34	303	2.39	42	1.86	1116	4.23
7	M	59	40	2.46	397	2.46	41	1.76	421	2.59	41	3.32	1464	3.02
7	M	63	42	2.36	238	2.36	41	1.54	260	2.57	44	3.04	1688	3.90
7	M	70	41	1.53	391	2.63	38	1.44	446	5.34	ns	0.60	1444	2.24
7	M	72	44	2.22	466	2.22	41	1.42	353	2.91	37	3.92	1645	3.39
7	M	77	43	2.15	548	2.15	43	1.54	501	1.67	40	2.50	1619	2.75
7	M	81	41	2.47	483	2.47	41	1.69	384	2.03	43	2.90	1785	4.45
7	M	89	44	2.82	ns	3.99	41	1.44	421	2.35	ns	1.36	1556	4.06

GROUP	SEX	ID #	Pre HCT	Pre AChE	Pre BuChE	Pre CaE	1° HCT	1° Post AChE	1° Post BuChE	1° Post CaE	7 Day HCT	7 Day AChE	7 Day BuChE	7 Day CaE
7c	M	47	46	2.36	371	2.13	41	1.78	439	2.13	ns	1.86	1725	3.09
7c	M	49	44	2.57	199	2.57	42	1.81	248	2.57	45	2.03	1369	3.90
7c	M	58	45	2.56	509	2.18	40	1.50	451	2.18	39	1.74	1678	3.51
7c	M	66	46	2.78	405	3.14	41	1.68	365	3.44	40	1.77	1397	3.32
7c	M	83	39	1.56	394	2.40	40	1.63	384	2.40	42	1.93	1560	5.48
7	F	92	45	1.24	ns	2.42	40	1.36	1869	2.19	43	ns	ns	ns
7	F	100	46	1.28	1571	2.46	44	1.38	2321	3.77	41	2.79	1999	2.95
7	F	102	44	1.73	839	2.27	38	1.34	1287	3.44	42	2.65	1828	2.64
7	F	106	43	1.78	1053	1.88	39	1.20	1330	1.72	41	2.30	2432	3.22
7	F	120	43	1.30	1233	2.51	40	1.18	1566	3.67	41	2.56	2983	3.01
7	F	125	46	1.49	1106	2.94	38	1.65	1770	3.66	38	2.67	2785	2.99
7	F	127	41	1.71	1045	2.74	39	1.35	2264	3.08	41	2.30	3435	2.62
7	F	131	47	1.40	1261	2.42	41	1.45	1999	3.14	40	2.52	2581	2.56
7	F	135	45	1.39	2347	2.58	40	1.20	2605	3.71	40	2.76	5600	3.16
7c	F	99	44	1.50	1582	2.97	39	1.41	1225	2.97	42	2.61	3954	6.82
7c	F	103	46	2.12	1195	4.12	38	1.48	2426	4.12	41	2.20	4647	5.69
7c	F	104	28	2.64	ns	3.25	40	1.43	1386	3.25	42	2.36	4443	4.36
7c	F	121	46	1.62	1425	3.86	40	1.26	1906	3.89	42	2.98	2847	2.85
7c	F	136	47	1.64	859	2.06	42	1.26	1201	2.56	43	2.56	2234	1.88
8	M	42	45	1.36	389	2.44	42	1.93	446	2.76	44	1.41	179	1.65
8	M	44	46	1.63	214	2.54	35	1.82	606	2.39	35	0.71	109	1.94
8	M	45	41	1.80	262	2.79	41	1.86	640	2.64	43	0.72	179	4.60
8	M	56	40	1.38	298	2.39	41	1.72	439	2.73	43	0.61	257	5.27
8	M	60	40	1.03	192	2.33	43	1.91	526	2.52	45	0.84	442	5.01
8	M	67	42	1.07	469	2.37	45	1.17	464	2.95	43	0.28	441	4.00
8	M	75	42	1.11	328	2.45	45	1.98	538	3.09	43	0.15	389	4.34
8	M	78	43	ns	387	2.70	36	1.76	551	2.40	42	0.63	153	NS
8	M	85	43	2.54	561	3.02	42	1.69	532	2.33	41	0.54	389	3.02
8	M	88	44	1.99	ns	ns	42	1.68	501	2.82	42	0.35	ns	ns
8c	M	54	40	2.36	557	3.92	42	1.78	532	2.98	41	0.46	6533	2.67
8c	M	64	41	2.30	370	2.30	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD	DEAD
8c	M	73	44	2.50	336	2.99	42	2.41	501	2.49	43	0.28	6059	2.52
8c	M	82	44	2.82	341	3.75	ns	ns	86	ns	45	0.75	6462	2.95
8c	M	86	42	2.24	385	3.30	45	1.89	483	2.44	45	0.48	6509	2.70
8	F	96	38	1.48	ns	2.30	42	1.57	1584	2.28	39	0.40	913	3.34
8	F	108	47	1.38	ns	2.76	42	1.21	2345	2.39	39	0.55	464	NS
8	F	113	47	1.51	ns	2.42	43	1.50	1330	2.14	38	0.13	1130	2.94
8	F	115	47	0.96	ns	1.64	44	1.37	2178	2.36	40	0.06	493	3.39
8	F	118	45	2.07	ns	3.16	45	1.67	3416	2.43	37	0.28	259	4.07

GROUP	SEX	ID #	Pre HCT	Pre AChE	Pre BuChE	Pre CaE	1° HCT	1° Post AChE	1° Post BuChE	1° Post CaE	7 Day HCT	7 Day AChE	7 Day BuChE	7 Day CaE
8	F	122	44	1.42	ns	2.64	42	1.37	4134	1.75	42	0.41	2997	1.84
8	F	130	43	2.13	ns	2.85	46	1.48	1807	2.28	41	0.50	2012	3.31
8	F	134	44	1.64	ns	2.92	43	1.44	2531	2.17	41	0.51	1942	2.92
8	F	138	49	1.51	ns	4.45	42	1.28	3119	2.44	37	0.73	2012	2.07
8	F	139	45	2.06	ns	3.01	42	1.50	2395	2.44	39	0.55	1701	3.07
8c	F	94	42	1.47	1107	2.93	46	1.59	1887	2.79	39	0.38	6511	2.59
8c	F	97	47	1.41	1139	2.01	41	1.52	2488	2.21	37	0.56	8074	2.81
8c	F	112	52	1.54	ns	3.54	44	1.43	2469	2.54	41	0.23	7677	2.44
8c	F	126	41	1.55	ns	1.85	42	1.44	3113	2.28	37	0.48	9589	2.78
8c	F	140	48	2.12	ns	3.29	44	1.42	3119	2.00	37	0.73	8972	2.99
9	M	196	41	0.91	272	3.21	38	0.81	1052	3.60	39	1.51	1299	2.12
9	M	206	45	0.35	1571	2.55	42	0.66	2587	3.46	ns	1.25	2227	1.68
9	M	211	44	0.64	1275	2.54	41	0.89	1828	3.04	ns	1.32	2227	1.56
9	M	213	47	0.61	390	2.76	39	1.07	988	3.26	41	1.37	978	1.41
9	M	214	41	0.91	559	2.46	41	0.94	1429	2.70	42	1.43	1219	1.67
9	M	226	46	0.84	421	3.08	40	0.36	1597	2.70	41	2.23	1602	2.24
9	M	227	45	0.83	330	2.17	41	0.87	789	3.17	39	1.45	1925	1.59
9	M	228	44	0.59	341	2.51	38	0.09	1396	2.95	40	1.27	2277	1.87
9	M	232	42	0.47	410	2.78	42	0.29	794	3.49	ns	2.12	1052	2.21
9	M	240	43	0.76	709	2.76	38	0.65	965	4.45	39	1.02	1448	2.04
9c	M	145	44	0.75	287	2.48	41	0.57	552	4.28	43	1.12	102	2.31
9c	M	152	43	0.67	341	2.39	40	0.42	524	4.05	44	ns	377	2.50
9c	M	174	42	0.42	413	2.15	40	0.22	568	3.66	ns	1.21	439	2.31
9c	M	176	41	0.57	282	2.30	39	0.73	394	3.51	ns	1.14	358	2.06
9c	M	190	43	0.50	284	2.91	40	0.78	513	4.20	40	1.36	347	2.32
9	F	143	41	0.93	296	2.21	41	0.32	388	3.67	41	1.66	519	2.12
9	F	147	44	0.83	310	2.49	43	0.08	257	4.84	41	0.89	266	2.05
9	F	151	44	0.74	408	2.49	40	0.58	320	4.02	ns	0.79	314	2.43
9	F	156	42	0.71	343	2.12	41	1.94	300	3.96	45	1.27	414	2.27
9	F	158	45	0.80	341	2.41	40	0.61	361	3.82	41	0.98	329	2.26
9	F	160	42	0.79	310	2.79	40	0.56	260	4.19	41	0.93	349	2.09
9	F	161	44	0.58	250	2.58	39	0.61	235	4.37	41	1.46	143	2.35
9	F	165	44	0.92	427	2.61	44	0.66	436	3.74	ns	1.57	390	2.06
9	F	172	48	0.74	413	2.55	43	0.10	340	4.19	44	1.22	342	2.44
9	F	186	43	0.77	307	2.60	39	0.76	343	4.14	45	0.94	458	2.28
9c	F	194	45	0.37	969	3.00	40	0.45	2265	3.35	41	1.27	1826	1.85
9c	F	198	46	0.50	236	2.91	40	0.86	1153	3.29	40	1.46	1429	1.60
9c	F	220	45	0.63	464	2.66	42	0.09	1657	3.23	ns	1.13	1628	1.39
9c	F	231	44	0.57	330	2.42	40	0.04	859	3.48	40	1.45	1194	1.87
9c	F	234	42	0.71	573	2.34	41	0.39	1429	3.24	40	1.13	1640	2.03

GROUP	SEX	ID #	Pre HCT	Pre AChE	Pre BuChE	Pre CaE	1° HCT	1° Post AChE	1° Post BuChE	1° Post CaE	7 Day HCT	7 Day AChE	7 Day BuChE	7 Day CaE
10	M	148	45	0.97	161	2.46	44	0.56	528	3.90	ns	0.77	446	2.69
10	M	157	43	0.88	250	2.44	41	0.39	297	3.85	ns	0.51	455	2.89
10	M	162	44	0.62	117	2.42	45	0.42	260	3.94	47	0.66	306	2.85
10	M	164	43	0.67	384	2.44	36	0.32	471	3.80	45	0.59	418	2.61
10	M	167	44	0.71	396	2.24	40	0.35	270	3.38	46	0.84	483	2.61
10	M	177	41	0.81	366	2.02	40	0.50	377	3.30	ns	1.12	455	2.68
10	M	179	43	2.09	366	2.26	42	0.34	334	3.66	41	0.50	798	2.81
10	M	181	39	0.70	282	1.95	40	0.03	333	3.32	43	0.62	594	2.25
10	M	184	43	0.80	226	0.37	43	0.20	108	3.93	44	0.84	511	3.05
10	M	189	43	0.92	542	2.68	39	0.60	452	3.32	45	0.80	675	2.50
10c	M	144	44	0.77	307	1.87	ns	0.63	ns	ns	45	0.66	492	2.53
10c	M	155	41	1.00	408	2.13	40	0.48	362	3.63	42	1.00	501	2.60
10c	M	166	46	1.06	451	1.75	39	0.46	291	3.29	43	1.02	873	2.55
10c	M	185	42	1.00	291	2.87	41	0.51	ns	3.72	44	0.77	473	2.45
10c	M	188	39	0.72	386	3.06	44	0.66	198	3.80	44	0.76	371	2.58
10	F	193	44	0.32	1451	3.02	43	0.31	1016	3.09	38	0.57	2414	2.24
10	F	201	49	0.59	666	2.77	40	0.48	670	3.11	39	0.71	1764	3.16
10	F	204	46	0.49	1035	2.44	44	0.46	1227	3.07	47	0.38	1105	2.41
10	F	205	49	0.29	844	2.77	42	0.25	667	3.22	41	0.54	1281	2.69
10	F	215	46	0.95	1432	2.80	42	0.23	1614	3.51	40	1.42	2617	2.15
10	F	216	42	0.99	1389	2.14	42	0.24	1269	3.69	47	1.28	2562	2.96
10	F	218	42	0.59	822	2.96	43	0.24	250	3.40	40	0.95	1439	2.14
10	F	223	43	0.60	660	2.79	41	0.08	730	3.00	43	1.77	2293	2.38
10	F	235	43	0.49	1002	2.71	40	0.04	1227	2.91	41	1.22	1262	2.46
10	F	236	44	0.32	1578	2.62	41	0.15	1902	3.01	43	1.71	3370	2.69
10c	F	197	42	0.53	1222	2.33	41	0.31	1182	2.87	42	0.51	2710	2.30
10c	F	199	50	0.64	1303	2.68	41	0.34	1012	2.87	39	0.51	2868	2.71
10c	F	209	46	0.66	707	2.55	ns	0.28	879	2.71	45	0.88	1374	2.73
10c	F	222	43	0.56	715	2.88	41	0.11	700	2.90	39	0.75	956	2.48
10c	F	237	45	0.37	999	2.88	46	0.54	780	2.68	41	1.51	1597	2.67
11	M	146	43	0.69	335	2.20	40	0.57	297	2.47	38	0.95	511	1.40
11	M	149	44	0.82	191	2.42	40	0.86	99	2.53	42	1.00	186	1.56
11	M	150	43	0.82	161	2.82	39	0.80	135	2.59	4?	0.77	258	1.70
11	M	154	44	0.81	317	1.91	41	0.57	146	2.32	40	1.11	334	1.64
11	M	159	44	1.00	281	2.27	41	0.79	139	2.44	ns	0.50	334	1.60
11	M	170	43	0.81	228	2.13	40	0.89	130	2.48	45	0.54	339	1.63
11	M	171	43	0.62	251	2.40	42	0.70	149	1.93	42	0.49	352	1.63
11	M	182	41	0.76	275	2.31	41	0.88	229	2.40	47	0.76	343	1.74
11	M	187	45	0.87	239	2.88	42	0.77	130	2.32	47	1.56	758	1.55
11	M	191	44	0.96	432	3.05	41	0.77	291	2.04	41	0.58	456	1.75

GROUP	SEX	ID #	Pre HCT	Pre AChE	Pre BuChE	Pre CaE	1° HCT	1° Post AChE	1° Post BuChE	1° Post CaE	7 Day HCT	7 Day AChE	7 Day BuChE	7 Day CaE
11c	M	153	42	1.49	414	2.88	41	0.74	213	2.25	42	0.77	334	3.26
11c	M	163	43	0.58	245	2.18	41	0.69	201	2.32	45	0.73	381	3.25
11c	M	175	43	0.52	252	2.37	41	0.57	99	2.78	45	0.80	278	2.99
11c	M	178	43	0.54	330	2.15	40	0.61	303	1.17	45	0.50	511	3.12
11c	M	180	45	0.48	263	2.24	42	0.57	229	2.08	45	0.27	381	3.74
11	F	192	43	0.60	1404	2.85	42	0.75	1516	1.85	ns	1.00	3527	2.47
11	F	195	45	0.47	1503	2.50	44	0.66	1708	2.05	44	0.27	4474	2.05
11	F	203	44	0.87	2614	2.62	37	0.64	2692	2.22	42	0.68	3088	2.22
11	F	207	47	0.51	2517	2.45	43	0.68	2704	1.85	40	0.43	4752	1.85
11	F	208	44	0.65	1379	2.88	41	0.74	1671	2.21	41	0.75	3175	2.21
11	F	212	43	0.71	2518	2.86	43	0.73	4313	2.04	43	1.66	5321	2.04
11	F	219	43	0.57	646	2.55	43	0.72	1448	1.75	44	0.50	1460	1.75
11	F	225	44	0.79	640	3.29	43	0.38	842	2.13	45	0.82	3391	2.13
11	F	233	42	0.67	1694	2.52	42	0.56	2123	1.90	31	1.52	3341	2.39
11	F	238	43	0.57	1069	2.55	45	0.64	2952	2.39	44	1.11	3541	2.44
11c	F	202	43	0.75	1297	1.55	40	0.59	1411.	2.33	41	0.89	2348	2.76
11c	F	210	45	0.55	1008	2.54	42	0.50	1120	2.34	ns	1.72	2120	4.38
11c	F	221	27	0.54	3252	2.18	41	0.44	2989	2.41	40	1.02	984	1.84
11c	F	229	44	0.69	998	2.61	42	0.37	2172	2.39	43	1.07	3249	2.22
11c	F	239	42	0.69	729	2.82	42	0.76	2048	2.66	ns	0.85	2557	3.01
12	M	244	40	0.88	246	1.28	40	0.90	235	3.49	41	0.70	381	2.73
12	M	245	44	0.81	254	1.31	43	1.00	161	3.03	44	0.95	239	2.94
12	M	248	41	0.55	192	1.84	38	1.32	415	2.18	37	0.59	323	2.54
12	M	250	39	0.94	241	ns	41	0.80	87	2.48	37	0.48	420	3.22
12	M	258	42	0.90	532	1.01	38	0.39	439	2.91	42	0.85	480	3.17
12	M	259	41	0.82	408	1.05	40	0.89	408	2.75	41	1.34	333	2.72
12	M	266	40	0.51	297	1.31	37	0.31	68?	4.80	ns	1.26	498	3.41
12	M	279	42	0.67	2.4?	1.21	39	0.65	464	3.81	ns	1.45	519	2.71
12	M	286	41	0.90	167	1.02	38	1.02	393	4.90	40	1.21	553	2.90
12	M	289	42	1.18	275	1.75	41	0.83	272	4.76	44	0.89	705	2.73
12c	M	243	41	0.89	396	1.22	43	0.42	328	3.10	40	1.03	354	2.99
12c	M	261	37	0.53	130	1.02	37	0.62	391	3.00	41	1.44	239	3.02
12c	M	271	41	0.99	266	1.12	39	0.27	105	4.17	41	1.69	544	4.28
12c	M	273	40	0.85	142	1.43	40	0.67	501	4.10	38	1.24	483	3.23
12c	M	290	41	0.61	125	1.47	39	0.83	179	3.84	42	1.33	400	3.09
12	F	297	38	0.58	869	1.67	37	0.55	1748	3.85	39	0.91	2475	2.79
12	F	299	45	0.72	405	1.86	30	0.85	319	4.88	41	1.01	1525	2.72
12	F	303	39	0.60	2416	1.64	37	0.46	1080	3.76	ns	1.38	2656	2.72
12	F	318	41	0.73	603	1.77	39	0.76	724	3.99	ns	1.09	1073	2.90
12	F	326	41	0.53	801	1.73	37	1.22	1356	4.26	37	1.14	2248	3.08

GROUP	SEX	ID #	Pre HCT	Pre AChE	Pre BuChE	Pre CaE	1° HCT	1° Post AChE	1° Post BuChE	1° Post CaE	7 Day HCT	7 Day AChE	7 Day BuChE	7 Day CaE
12	F	328	39	0.56	653	1.44	37	0.76	337	4.45	42	0.34	2034	3.32
12	F	331	39	0.89	733	1.68	37	0.85	272	3.50	39	1.02	1779	3.11
12	F	333	45	0.59	578	1.81	39	0.68	708	6.32	ns	0.53	1660	3.84
12	F	337	42	0.63	887	1.74	38	1.06	653	4.10	40	1.10	2682	3.00
12	F	340	41	0.82	6.58?	1.20	39	1.17	708	2.83	ns	2.56	1549	1.95
12c	F	296	39	0.78	492	1.88	38	0.56	616	3.62	ns	1.35	1243	2.73
12c	F	317	41	0.59	1167	1.61	38	0.29	736	ns	41	1.23	ns	4.39
12c	F	305	43	0.60	486	1.57	31	Ns	430	4.37	36	1.62	658	3.89
12c	F	334	43	0.51	584	1.64	40	0.83	1380	4.13	40	0.83	1246	3.29
12c	F	338	41	0.80	1339	1.67	31	0.85	440	3.82	39	1.02	2648	2.88
13	M	247	40	0.81	303	0.75	39	0.36	291	3.97	42	0.41	538	3.68
13	M	256	41	0.68	248	1.46	41	0.63	281	3.39	46	1.07	517	2.86
13	M	257	40	0.81	309	1.18	40	0.54	290	4.40	ns	1.02	464	3.31
13	M	260	39	0.56	192	4.30	40	0.26	114	3.35	44	1.05	297	2.83
13	M	262	40	0.65	179	1.42	41	0.20	225	3.17	ns	0.85	299	2.66
13	M	263	40	0.72	328	1.00	41	0.28	198	4.02	41	0.56	381	3.21
13	M	265	37	0.84	390	1.22	41	0.30	415	3.71	ns	0.80	1021	3.17
13	M	280	42	0.73	210	0.88	40	0.06	235	3.78	41	0.73	306	3.33
13	M	283	38	0.80	198	0.94	40	0.22	281	3.65	42	0.94	566	3.17
13	M	287	39	0.73	232	1.62	40	0.55	309	3.61	46	0.78	640	2.96
13c	M	270	38	0.84	303	1.23	42	0.54	281	4.37	40	0.76	705	3.27
13c	M	276	42	0.87	266	1.20	39	0.53	290	3.63	39	0.71	650	3.44
13c	M	277	39	0.97	309	1.10	43	0.22	328	3.57	43	0.81	594	3.30
13c	M	282	39	0.86	328	1.29	40	0.85	365	4.12	43	0.99	678	3.37
13c	M	285	37	0.77	167	0.83	39	0.54	393	2.98	41	1.34	678	2.58
13	F	294	39	0.70	319	1.55	41	0.70	1949	2.19	44	1.17	2394	2.56
13	F	300	39	0.93	629	1.75	44	0.31	2098	2.19	42	0.81	1753	2.61
13	F	302	42	0.73	1631	1.45	41	0.36	2933	1.92	45	0.58	5012	2.54
13	F	307	41	0.83	616	1.45	43	0.57	2525	2.27	42	0.70	3602	3.07
13	F	312	40	0.70	288	1.66	44	0.62	1030	2.53	42	0.39	854	3.47
13	F	320	41	0.74	956	1.38	44	0.31	2098	2.17	44	1.00	2970	3.40
13	F	324	40	0.58	610	1.57	42	0.61	1986	2.33	44	1.20	1986	2.89
13	F	330	42	0.58	950	1.60	43	0.60	2191	2.54	42	0.71	2413	3.71
13	F	332	40	1.01	647	1.50	40	0.63	2107	2.25	46	0.56	2135	3.08
13	F	335	41	0.69	807	1.53	42	0.77	2191	2.63	41	1.04	2163	3.22
13c	F	293	41	0.70	832	1.46	46	0.74	3370	2.38	46	1.05	3824	2.32
13c	F	322	41	0.60	659	1.38	41	0.78	1838	2.36	41	1.03	1986	2.88
13c	F	323	40	0.68	733	1.62	41	0.90	3045	2.34	41	1.22	3852	4.05
13c	F	325	43	0.71	764	1.64	45	0.77	3082	2.63	45	1.31	3713	2.94
13c	F	341	ns	0.91	553	1.41	42	1.04	3583	2.19	42	0.76	3444	2.30

GROUP	SEX	ID #	Pre HCT	Pre AChE	Pre BuChE	Pre CaE	1° HCT	1° Post AChE	1° Post BuChE	1° Post CaE	7 Day HCT	7 Day AChE	7 Day BuChE	7 Day CaE
14	M	242	40	0.97	211	1.39	42	1.56	654	2.03	45	0.71	524	3.04
14	M	246	41	1.20	316	1.33	42	0.92	682	2.22	46	0.53	552	3.65
14	M	252	41	0.84	272	1.33	42	0.70	710	2.91	44	0.48	524	4.25
14	M	253	39	0.86	495	1.30	31	1.25	1156	2.76	46	0.61	803	4.72
14	M	267	41	0.73	291	0.86	42	1.05	757	2.47	32	0.54	483	3.57
14	M	268	40	0.73	384	0.87	43	1.04	636	2.11	46	0.52	436	3.45
14	M	269	41	0.64	452	1.37	41	0.63	849	2.54	44	0.91	701	3.79
14	M	272	41	1.20	254	1.30	42	0.46	654	2.55	45	0.82	432	3.33
14	M	284	39	0.74	198	0.94	45	0.82	608	1.90	45	0.77	413	2.75
14	M	291	40	0.72	350	1.97	44	0.77	654	2.21	44	0.79	478	3.81
14c	M	249	41	0.66	341	1.06	41	0.96	654	2.60	43	0.80	404	3.85
14c	M	274	41	0.64	111	1.15	42	0.45	515	2.68	39	0.66	436	2.77
14c	M	278	40	0.83	266	0.94	43	0.79	682	ns	46	0.68	404	3.58
14c	M	281	41	0.81	254	1.28	44	0.78	543	2.19	44	0.55	302	3.43
14c	M	288	43	1.02	251	1.75	42	1.14	589	2.63	43	0.73	339	3.99
14	F	292	41	0.82	1513	1.55	42	1.21	5291	2.33	43	0.82	5574	3.40
14	F	295	38	0.61	313	1.60	42	1.18	1736	3.34	42	0.27	1740	3.39
14	F	298	41	0.72	696	1.47	41	0.90	3008	2.54	39	0.38	3012	3.24
14	F	306	39	1.54	727	1.49	44	0.74	3435	2.82	42	0.79	3829	3.15
14	F	308	42	0.63	430	1.62	43	0.70	1522	2.42	27	0.84	1221	3.40
14	F	311	42	0.79	826	1.11	42	1.77	3648	2.05	39	2.09	2337	2.73
14	F	314	41	0.83	1284	1.25	41	1.32	3388	1.91	40	1.65	3625	2.91
14	F	316	44	0.61	1297	1.60	44	1.00	3156	2.15	40	0.42	2604	3.37
14	F	321	40	0.58	628	1.58	43	1.40	2005	2.50	39	0.36	1954	2.28
14	F	339	42	0.77	1060	1.36	40	2.88	2887	2.33	38	0.92	2659	3.19
14c	F	309	41	0.60	560	1.48	41	0.86	2785	2.45	40	0.77	2195	3.47
14c	F	310	40	0.58	511	1.32	40	0.82	2488	2.29	41	1.67	1936	2.91
14c	F	313	41	0.94	517	1.54	44	0.88	2311	2.53	38	1.06	2214	3.07
14c	F	315	46	0.73	832	1.33	42	0.93	3137	2.29	39	0.86	2994	3.09
14c	F	336	41	0.79	1029	1.38	41	1.36	2757	2.50	37	0.88	2743	3.34
15	M	345	45	1.58	223	3.60	42	0.59	204	3.09	43	0.41	348	2.98
15	M	346	45	1.49	223	3.33	40	0.53	213	3.01	ns	0.62	394	2.67
15	M	348	45	1.49	353	3.16	41	0.45	316	3.16	38	0.59	413	2.56
15	M	357	44	2.07	353	3.42	40	0.08	381	3.41	43	1.14	571	2.56
15	M	363	46	1.78	436	3.96	42	0.65	362	3.94	42	0.80	376	2.40
15	M	369	39	2.14	455	3.39	41	0.56	427	3.77	45	0.41	626	3.39
15	M	370	44	1.83	408	2.64	41	0.57	390	2.96	42	0.46	673	3.03
15	M	373	41	1.99	316	2.64	44	0.45	325	3.10	43	0.43	506	3.68
15	M	374	43	1.91	288	3.41	41	0.58	369	2.70	42	0.48	348	2.49
15	M	388	43	1.79	325	3.13	41	0.55	306	2.44	42	0.45	476	2.55

GROUP	SEX	ID #	Pre HCT	Pre AChE	Pre BuChE	Pre CaE	1° HCT	1° Post AChE	1° Post BuChE	1° Post CaE	7 Day HCT	7 Day AChE	7 Day BuChE	7 Day CaE
15c	M	343	47	1.66	241	4.27	41	1.10	418	3.56	43	1.84	469	3.01
15c	M	353	47	1.02	408	3.21	41	0.87	511	2.96	ns	0.29	636	2.98
15c	M	356	44	1.73	399	3.04	39	0.62	371	3.11	ns	0.51	459	2.43
15c	M	361	44	1.90	362	4.05	39	0.84	381	3.62	41	0.54	454	2.91
15c	M	372	46	1.67	214	4.26	42	0.75	390	4.32	42	0.75	441	2.02
15	F	392	46	1.65	1151	3.01	39	1.62	1145	3.75	33	1.70	1253	1.52
15	F	393	43	1.79	1513	2.83	41	1.58	1795	3.47	26	1.29	1578	2.20
15	F	406	46	0.44	2348	3.29	41	1.57	1433	3.71	26	0.83	1095	2.05
15	F	418	43	0.79	1076	3.01	39	1.54	1545	3.60	41	1.24	1541	2.49
15	F	422	43	0.58	2850	2.94	42	1.07	2120	3.81	41	1.73	1949	1.85
15	F	423	49	0.65	984	2.33	41	1.30	3011	3.07	28	1.37	2618	1.85
15	F	428	42	0.87	891	3.72	39	1.40	1238	3.77	37	1.26	1253	2.55
15	F	438	40	0.86	1318	3.71	41	1.32	2092	2.43	43	1.33	2432	1.64
15	F	440	48	1.61	1253	2.83	43	1.14	2027	3.34	32	1.80	1550	2.18
15	F	441	44	1.92	1522	2.87	39	1.51	1832	3.35	41	1.62	1727	2.17
15c	F	404	44	0.82	1587	3.08	42	0.79	2267	3.29	29	0.52	640	1.68
15c	F	419	46	0.71	1532	3.16	40	1.97	1775	2.95	41	1.12	752	1.93
15c	F	421	46	0.61	1624	3.05	40	1.79	2582	3.78	42	1.79	1012	2.46
15c	F	430	34	0.96	2404	2.69	40	2.20	2015	3.02	38	1.65	1309	2.01
15c	F	434	45	0.63	1030	3.34	37	1.74	2063	3.18	ns	ns	1290	1.87
16	M	342	44	1.43	353	3.94	36	1.91	399	ns	41	0.83	487	3.64
16	M	352	48	1.79	325	3.50	40	1.78	278	3.27	47	0.81	459	2.42
16	M	354	46	1.75	381	4.26	42	1.98	288	3.53	43	0.50	506	2.82
16	M	355	44	1.62	371	3.55	37	1.42	269	2.61	39	1.07	441	1.27
16	M	359	47	1.72	362	3.60	44	1.67	455	3.53	41	0.89	515	3.12
16	M	367	43	1.66	316	3.83	39	3.17	362	3.58	42	0.74	543	2.76
16	M	379	43	1.33	232	3.54	40	1.47	362	3.16	43	0.64	580	2.29
16	M	382	39	1.74	390	3.91	36	0.97	557	3.31	43	0.91	775	2.83
16	M	383	42	1.81	353	3.15	41	1.22	640	2.90	45	0.87	654	3.56
16	M	391	44	1.55	251	3.61	40	1.72	353	3.09	43	0.72	450	2.24
16c	M	350	45	1.62	260	3.49	39	1.99	278	3.06	ns	1.42	459	2.71
16c	M	358	45	1.92	408	3.89	41	1.96	678	3.08	40	0.78	784	2.90
16c	M	362	41	1.91	381	2.88	43	1.95	640	3.90	37	0.71	589	2.40
16c	M	376	39	1.78	334	3.23	44	2.10	501	3.79	39	0.64	552	1.97
16c	M	387	39	2.32	501	3.08	40	2.15	808	3.15	41	0.62	886	3.57
16	F	397	42	2.25	743	2.94	38	1.22	678	3.08	43	1.80	1244	2.44
16	F	411	46	1.10	1940	3.46	39	1.42	1439	3.29	32	0.83	1921	2.03
16	F	414	48	1.28	1318	3.94	41	1.29	900	4.00	33	1.22	1151	2.66
16	F	415	45	0.82	1857	2.34	40	1.37	1086	2.45	33	1.30	1476	1.67
16	F	416	46	0.44	1040	2.57	39	1.60	1652	3.52	34	1.26	1773	2.55

GROUP	SEX	ID #	Pre HCT	Pre AChE	Pre BuChE	Pre CaE	1° HCT	1° Post AChE	1° Post BuChE	1° Post CaE	7 Day HCT	7 Day AChE	7 Day BuChE	7 Day CaE
16	F	420	45	1.27	1634	2.86	39	1.44	1782	3.50	ns	1.43	1801	2.36
16	F	424	47	0.66	ns	3.10	38	2.07	975	3.06	31	1.22	965	1.90
16	F	431	44	1.18	1949	3.00	37	1.74	1986	3.50	41	1.58	1912	2.21
16	F	432	45	1.93	1430	2.58	36	1.97	1309	2.53	40	1.90	1875	1.90
16	F	433	46	0.73	1689	3.37	39	1.71	1327	3.29	41	1.34	1532	2.66
16c	F	395	44	1.94	1894	2.01	42	1.43	2190	2.27	42	1.46	3314	1.72
16c	F	398	49	1.49	483	3.53	34	0.72	965	3.07	34	2.07	900	1.92
16c	F	401	48	1.85	910	2.28	ns	1.65	2163	3.43	40	1.48	2497	1.95
16c	F	426	48	0.66	863	3.01	42	2.77	1197	3.43	42	1.51	1596	2.39
16c	F	437	40	0.74	1309	2.75	35	1.44	1522	2.93	35	1.33	1522	1.80
17	M	344	44	1.89	269	4.24	40	0.53	218	2.63	46	0.99	557	2.73
17	M	347	45	1.58	381	3.37	42	0.64	283	2.38	43	1.64	473	2.14
17	M	360	45	1.68	260	3.38	43	0.37	367	3.87	43	1.30	560	3.05
17	M	364	40	1.80	186	3.90	39	0.46	209	3.22	46	1.49	343	2.80
17	M	371	42	1.73	371	3.00	43	1.26	357	3.52	46	1.53	436	2.47
17	M	378	40	1.33	251	3.76	39	0.30	200	2.80	44	0.79	427	2.74
17	M	381	41	1.86	371	4.52	41	0.18	274	3.01	46	1.29	436	2.97
17	M	384	43	1.71	269	3.56	39	0.43	162	2.78	44	0.79	640	3.00
17	M	386	47	1.74	381	3.61	44	0.30	236	2.66	47	0.60	631	2.90
17	M	390	43	1.50	306	4.27	41	0.23	348	3.09	46	1.26	515	3.09
17c	M	365	42	1.79	316	3.12	39	0.48	357	2.59	45	1.84	446	2.27
17c	M	377	44	1.82	325	3.62	40	0.70	320	2.79	48	0.78	427	2.69
17c	M	380	43	1.49	422	3.93	40	0.24	506	2.63	47	0.46	436	2.78
17c	M	385	40	1.69	297	3.66	40	0.59	385	3.33	45	0.59	631	2.83
17c	M	389	44	1.80	353	3.50	40	0.57	422	3.03	45	1.05	464	2.96
17	F	394	46	1.94	1959	3.37	41	1.45	2184	3.03	44	0.53	2998	1.72
17	F	396	49	1.55	1281	3.49	44	0.85	1015	3.22	45	0.17	1225	2.15
17	F	400	49	2.09	1699	3.21	44	1.88	2825	2.38	41	0.12	3313	1.84
17	F	407	44	0.59	825	3.38	41	0.76	2760	2.95	43	1.54	3314	1.83
17	F	408	45	1.13	2144	4.05	41	0.75	1832	2.96	38	0.51	2321	2.32
17	F	409	47	1.49	1300	2.88	42	1.87	1433	2.56	32	0.31	2163	2.40
17	F	412	47	0.89	1532	3.12	42	1.51	2101	2.92	38	0.24	2757	2.08
17	F	429	41	0.90	975	3.91	41	1.57	1266	3.79	43	0.25	1949	2.51
17	F	435	44	0.76	1355	3.13	40	1.35	1553	2.47	30	0.23	1986	1.86
17	F	439	44	1.13	1300	3.31	40	0.80	1590	2.83	ns	0.17	1912	1.89
17c	F	402	44	1.19	1726	3.55	38	1.76	1414	3.08	42	0.31	1736	2.21
17c	F	403	41	0.99	891	3.04	41	1.13	2036	3.09	43	1.26	3376	2.15
17c	F	410	45	0.75	1204	3.96	38	0.62	1405	2.90	30	0.11	2738	2.15
17c	F	413	47	1.30	947	3.53	42	1.33	1442	3.07	43	0.12	1513	2.35
17c	F	425	44	0.71	1309	3.76	41	1.46	1627	3.12	38	0.15	1587	2.11